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J. LEON LASCOFF.

J. Leon Lascoff was born in Russia on August 28, 1867. He received his academic and professional education in his native land and then came to the United States, arriving in New York in May 1892. During the seven years, 1892–1899, he was employed as clerk in the well-known pharmacies of D. Hayes and Sons, Merck & Co. and Dr. Gustav Pfingsten, and on March 11, 1899, he opened his own pharmacy on Lexington Avenue, building up the magnificent professional pharmacy which represents the best traditions of our calling. It was Dr. Lascoff's great joy to compound on November 29, 1936, the millionth prescription dispensed at his pharmacy; now the firm of J. Leon Lascoff & Son.

Becoming a registered pharmacist of the State of New York in 1893, Dr. Lascoff has had the honor of serving on the State Board continuously from 1910 to date. He has been honored with the Presidency of the Board during no less than three terms (1914, 1921 and 1929). His work in connection with the committee of practical examinations has been particularly noteworthy.

Dr. Lascoff is a great organization man, ever striving to be of service to his fellow pharmacists and also to his less fortunate neighbors of the great city, of which he is a highly esteemed resident. He has been selected as pharmaceutical representative of the "drive" committees of the Red Cross, the Salvation Army, the Emergency Unemployed Relief Committee. He is a member of the New York Board of Trade and one of its directors; he has been vice-president of the Yorkville Chamber of Commerce; he is a member of the advisory board of the New York City Board of Health.

As to pharmaceutical organizations, he has been a member of the New York State Pharmaceutical Association since 1900, in which he has performed valiant service as chairman of the U. S. P. and N. F. Propaganda Committee since 1914. He was the organizer of the New York County Pharmaceutical Society in 1911 and served as its president during two years (1911–1913). He has been a member of the Board of Trustees of Columbia University College of Pharmacy since 1916. He was one of the organizers of the New York Veteran Druggists' Association and

has been its treasurer since its inception. He is honorary member of several of the many retail drug associations of Greater New York.

Dr. Lascoff has added much of great value to pharmaceutical literature. His bibliography now numbers 156 titles. He served as prescription editor of the *New York Journal of Pharmacy* and now occupies the same position on the staff of *Drug Topics*.

Dr. Lascoff's services to the AMERICAN PHARMACEUTICAL ASSOCIATION have been manifold. He became a member of our ASSOCIATION in 1903 and was chairman of our Section on Practical Pharmacy and Dispensing in 1913. In 1920 he became chairman of the Recipe Book Committee and has performed outstanding work on this great undertaking ever since. We are proud and happy to acclaim his scientific and executive ability in directing the work of his well-chosen committee in preparing this valuable book, in the name of the A. PH. A. for the benefit of the practicing pharmacists of America. It can truly be said that R.B.I and R.B.II stand as monuments to our good friend, Dr. Lascoff.

It is difficult to close this tribute to Dr. Lascoff. His beautiful family relations, his gracious wife, his outstanding son and charming daughter-in-law and his lovely brand-new grandson should be discussed at length. His fine services from 1920 to date as a member of the Revision Committees of the U. S. P. X and XI deserve more than these few lines. Finally to those who hold him dear, the topic "Lascoff, the friend," would require pages.

In 1937 he was awarded the first honor plaque of the *American Druggist* as the outstanding retail druggist of the State of New York.—H. V. A.

THE HUMAN ADVENTURE.

An event of the Atlantic City program, American Association for the Advancement of Science, was the showing of "The Human Adventure." This eight-reel talking picture was produced under the personal supervision of the late Professor James Henry Breasted[1] and was planned to show the rise of man from savagery to civilization. The sound record in the second reel is in the voice of Dr. Breasted himself, and the entire film was produced at the Oriental Institute of the University of Chicago. The story was written and, except for the second reel, told by Mr. Charles Breasted. A large audience, in which were many former colleagues and old friends of Dr. Breasted, saw the film, which was exhibited through the courtesy of Wendell G. Shields, of New York City.—From *Science*, February 5, 1937.

Dr. Henry B. Ward, after many years of service, asked to be relieved as permanent secretary of the Association for the Advancement of Science. Resolutions of appreciation were passed.

Dr. Frederick J. Wulling was elected emeritus member.

NATIONAL INSTITUTE OF HEALTH.

A step toward establishing the National Institute of Health, to be located beyond Bethesda, Md., has been taken.

From a beginning, with the animal house, which is to be used also for other purposes, it has been the general intention that the site be developed eventually to take over all the National Institute of Health, now located in Washington just west of the Naval Hospital.

Eventually, when this is done, the buildings now occupied there by the National Institute of Health would be turned over to the Naval Hospital, for part of the great center of national defense, in that section of the city, near which is located the AMERICAN INSTITUTE OF PHARMACY, will some day include the new War Department, a new Navy Department and Naval Museum.

[1] A graduate of Chicago College of Pharmacy.

EDITORIAL

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SOME EPOCHS OF PHARMACY.

"SOME Epochs in Medical Science" was the subject of an important contribution to the program of the American Association for the Advancement of Science at Atlantic City, by Dr. W. M. Stanley of Rockefeller Institute for Medical Research.

The Glycerin Producers' Association is celebrating the anniversary of Scheele's discovery of glycerin, a very worthy tribute to the discoverer of a product which has many uses, but this is only one of Scheele's many discoveries which have contributed to the industries, arts and professional services.

In a radio address, about five years ago, Dr. Howard W. Haggard said, in part—The trust of Scheele's neighbors "was a sincere tribute to the pharmacist—for it was solely as a pharmacist that these people knew him. They did not recognize that he was a man destined to become a world figure in science. Nor was such fame sought by Carl Scheele; his life was devoted to pharmacy and service to his community." He refused a place on a University faculty, because he feared that the acceptance would interfere with his research. The address is quoted further in the following: "In his spare time, the moments when there were no prescriptions to fill, when there was no one to seek his service, and the lights of his modest pharmacy were dimmed for the night, he worked to satisfy his own insatiable curiosity concerning the materials with which he dealt." Observation, experimentation and sacrificing devotion gained for him surpassing eminence and pharmacists should never overlook the opportunity of having part in the work of their co-workers, without a purpose to take from the industries a share in the honors of achievement by pharmacists.

An article on Pasteur is quoted in the following: "Louis Pasteur revolutionized medicine by discovering and proving the germ theory of disease. It might be asserted with reason that Pasteur did more for mankind than any other one man." Other discoveries were referred to and rightly so, but it is not mentioned that Pasteur was Assistant Professor at the Strasbourg School of Pharmacy, that he was assistant in Balard's laboratory, that he won a prize of the Societé de Pharmacie de Paris, half of which he devoted to purchasing certain necessary apparatus with which he carried on further investigations.

The article referred to Sir J. Y. Simpson and his discovery of the efficacy of chloroform in surgery and the use of ether, but it is not mentioned that a large part of the work was carried on in a British Pharmacy; the discoveries of Morton and Long are spoken of, but it is not stated that without the persistent efforts and loyalty of a pharmacist to his preceptor, an apprentice in the "drug shop" of Dr. C. W. Long, the recognition to the latter would not have been given.

T. H. Huxley was ever ready to speak of the pharmacists' part in the development of materia medica and his early experience in a pharmacy.

The pharmacy prize to Group II was given for a Cinchona display, in which Caventou and Pelletier had an outstanding part and the research was carried on in their pharmacy.

Because the researches of our present-day pharmacists are so near, we do not look upon them as outstanding, but some of the results will be so reported in later years, and unless we keep them in mind and lay claims for pharmacy, credit will be given to other divisions of research. Pharmacy has its epochs and pharmacists have duties in higher conceptions and responsibilities. Liberty is taken in referring to page 963 of the November JOURNAL.

A NOTE FROM THE U. S. P. ON THE ASSAY FOR CALCIUM IN BLOOD SERUM.*

UNDER *Solution of Parathyroid* of the Pharmacopœia, page 216, an assay is provided to indicate the potency of the Solution. Certain details are supplied under the assay, the latter being dependent upon the increase of the calcium content of the blood serum of dogs into which the Solution has been injected.

Standards have been established but it was not considered necessary when the monograph was prepared to incorporate the exact technique for determining the quantity of calcium in the blood of the test animal. It has been pointed out, however, that various methods for making this determination have been used and that for uniformity in both the standardization of the official product and in the subsequent estimation of its potency, it is important to employ the same procedure.

For this reason the Sub-Committee on Biological Assays, of which Dr. C. W. Edmunds is Chairman, has prepared the details of an assay suitable for pharmacopœial adoption. It is proposed that this assay, or something very similar to it, be introduced into the Pharmacopœial text in one of the future Supplements. In the meanwhile, it is being placed in the pharmaceutical literature so that it may be available for users of the Pharmacopœia in making this determination.

It is hoped that the detailed procedure will be tried by many laboratories and its efficiency thoroughly demonstrated before it becomes official. Those who try this test are invited to correspond with the Chairman of the Committee of Revision, indicating the results obtained.—E. FULLERTON COOK, *Chairman*, U. S. P. Committee of Revision.

OPIUM CONTROL.

The system of international control over narcotic drugs which the United States has advocated and supported for many years is threatened by the menace of opium in the Far East, according to a report by Frederick T. Merrill, published by the Foreign Policy Association.

The report declares that China's latest antiopium campaign has reached its most sensational stage with the threatened execution of hundreds of drug addicts and peddlers, but it points out that the effectiveness of the Nanking government's opium drive has not yet been demonstrated by action on the entire program. The United States, according to Mr. Merrill, is especially concerned by evidence tending to show that increasing amounts of drugs seized on the Pacific Coast originate in the Orient. . . .

The report concludes that "the success of China's latest efforts to combat the opium problem, which are embodied in the 'six-year plan' for the suppression of opium, is dependent on the Nanking government's ability to enforce its laws in general, its willingness to enforce the opium regulations in particular, its progress in re-orienting its agricultural economy away from opium, and its readiness to eliminate opium revenue as a source of public and private income. Only a partial advance has been made, but apparently the central government is increasingly sincere in its efforts to eradicate opium. . . ."

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* See page 259.

SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, F. E. Bibbins; H. M. Burlage, W. G. Crockett, E. V. Lynn, C. O. Lee, L. W. Rising, L. W. Rowe, Heber W. Youngken, F. V. Lofgren, J. C. Krantz, Jr.

PREPARATION OF DIVINYL ETHER.

BY W. A. LOTT, F. A. SMITH AND W. G. CHRISTIANSEN.[1]

During the last decade, since the substance $\beta\beta'$-dichloroethyl ether has become readily accessible, the preparation of divinyl ether from it has been accomplished by three groups of workers.

Cretcher and Pittenger (1) were the first to accomplish this. They made the interesting discovery that the reaction between $\beta\beta'$-dichloroethyl ether and the sodium alcoholates of certain primary alcohols of low molecular weight, carried out by refluxing in an excess of the alcohol, did not result in the withdrawal of hydrogen chloride from the dichloroethyl ether to form divinyl ether, but proceeded by the mechanism of the Williamson synthesis to give the ethers of the general formula $ROCH_2CH_2OCH_2CH_2OR$, or, when an excess of the $\beta\beta'$-dichloroethyl ether was present, the half ethers $ROCH_2CH_2OCH_2CH_2Cl$. In this manner they produced in good yield the ethers

β-chloro-β'-methoxy diethyl ether
Bis (β-methoxy) diethyl ether
Bis (β-ethoxy) diethyl ether
Bis (β-propoxy) diethyl ether
Bis (β-butoxy) diethyl ether

They found, however, that when $\beta\beta'$-dichloroethyl ether was digested with heated sodium hydroxide without the presence of an hydroxylated solvent it suffered the loss of one or two molecules of hydrogen chloride to give some vinyl ethyl ether and some divinyl ether. They reported also the formation of acetaldehyde as a by-product.

Hibbert, Perry and Taylor (2) confirmed the findings of Cretcher, *et al.*, in that they too obtained vinyl ethyl ether, divinyl ether and acetaldehyde when $\beta\beta'$-dichloroethyl ether was digested with solid potassium hydroxide at elevated temperatures.

Ruigh and Major (3) improved the method of Hibbert (2), *et al.*, by adding the $\beta\beta'$-dichloroethyl ether gradually to the vigorously agitated molten potassium hydroxide. In this way they were able to obtain yields of 21% and better of divinyl ether. By the use of suitable apparatus they effected a fractionation of the products of the reaction so that a considerable portion of the chloroethyl vinyl ether refluxed back into the reactor while the divinyl ether as well as the low boiling impurities, *viz.*, acetaldehyde and ethylene oxide continued on to a condenser in which all but the gaseous impurities were finally condensed. They also found that a small stream of gaseous ammonia continuously passed through the system repressed the formation of acetaldehyde somewhat.

[1] Research Department of the Chemical and Pharmaceutical Laboratories, E. R. Squibb & Sons, Brooklyn, N. Y.

In considering the experiences of these several authors it seemed at the outset that a method by which the withdrawal of two molecules of hydrogen chloride from the $\beta\beta'$-dichloroethyl ether could be carried out by means of potassium hydroxide or a similar alkaline substance in a homogeneous reaction mixture through the use of a suitable solvent would be much more controllable and might obviate to a large degree the many possible side reactions. To devise such a method we needed to provide a solvent which could dissolve an alkali such as potassium hydroxide as well as the organic substance $\beta\beta'$-dichloroethyl ether. Only an hydroxylated solvent such as an alcohol could be expected to do this and we therefore subjected a quantity of $\beta\beta'$-dichloroethyl ether to the action of alcoholic potassium hydroxide. It was found, however, that here, too, a condensation reaction occurs between the dichloroethyl ether and the alcohol to give Bis (β-ethoxy) diethyl ether and no withdrawal of hydrogen chloride to give divinyl ether. Further consideration of the subject, however, suggested the use of such alcohols, or hydroxylated solvents in general, which would not react according to the Williamson synthesis due either to excessive molecular weight or some structural peculiarity. In general an alcohol of C_5 or greater would be expected to form ethers by condensation with alkyl halides (Williamson synthesis) only with great difficulty. Also one would expect secondary alcohols to form ethers by this mechanism with considerable difficulty; and tertiary alcohols almost not at all. In addition to non-participation in the Williamson reaction a suitable hydroxylated solvent is needed to fulfil the additional requirement of dissolving generous concentrations of potassium hydroxide as well as the dichloroethyl ether. It was expected that this difficulty would be hard to meet for it was not at all to be expected that an alcohol of C_5 or more would dissolve any significant quantities of potassium hydroxide. For this reason it was decided to make the first attempt with the dihydroxylated solvent, diethylene glycol ($\beta\beta'$-dihydroxy ethyl ether); and, we were able to obtain a yield of 25% of divinyl ether by the gradual addition of dichloroethyl ether to a refluxing solution of potassium hydroxide in this solvent.

This experiment was of considerable interest in that we were able to obtain yields of divinyl ether comparable to those of Ruigh and Major (3) despite the fact that we were using potassium hydroxide dissolved in an alcohol, the alcohol having been so chosen that the difficulty due to etherification reported by them was obviated. The method was not altogether satisfactory, however, since the yield of divinyl ether was not markedly increased over theirs and since the formation of acetaldehyde and gaseous decomposition products was not eliminated.

Our attention was then attracted to a rather interesting primary octyl alcohol, *viz.*, 2-ethyl hexyl alcohol, which had recently become an article of commerce. Its high molecular weight seemed to exclude any probability of its undergoing ether formation and we therefore determined the solubility of potassium hydroxide in this solvent. We were considerably surprised to find that this solubility was about 6% at 110° and became considerably higher as the temperature was elevated above that point. In an experiment in which dichloroethyl ether was added to a solution of potassium hydroxide in 2-ethyl hexyl alcohol we obtained a yield of 31–32% divinyl ether with almost no acetaldehyde or other volatile impurities in the distillate. Control of the reaction was at no time difficult and purification of the crude yield a very simple matter. The apparatus can be set up out of ordinary

laboratory glassware in very short time and the experiment carried out in a few hours.

In view of the fact that interference with these reactions due to ether formation did not occur, it was now decided to attempt the elimination of hydrogen chloride from the dichloroethyl ether to form divinyl ether by means of sodium alcoholates dissolved in an excess of the corresponding alcohols. In doing so we again avoided the primary alcohols of low molecular weight such as were used by Cretcher, *et al.* (1), and again selected such alcohols as would be expected to resist etherification by the Williamson reaction. Tertiary butyl, tertiary amyl and tertiary hexyl alcohols were chosen because of their tertiary stucture, and the primary alcohol 2-ethyl hexanol due to its high molecular weight. In the case of tertiary butyl alcohol only a very poor yield of divinyl ether was obtained. Possible reasons for this poor result were the low attainable reaction temperature or the low solubility of sodium tertiary butyl alcoholate in that alcohol. The addition of dichloroethyl ether to solutions of the corresponding sodium alcoholates in all of the other alcohols, however, gave very satisfactory yields of divinyl ether. Due to the absence of side reactions the crude product contained only traces of acetaldehyde or other volatile impurities so that its purification was a very simple matter. Practically no gaseous decomposition products were formed, so that the reaction and delivery of product were at all times smooth and controllable.

It should be added that in no case did we try to extend our experiments beyond preliminary stages so that the results reported including yields are all amenable to considerable improvement by further study.

EXPERIMENTAL.

1. First Method—Reaction between $\beta\beta'$-dichloroethyl ether and potassium hydroxide dissolved in diethylene glycol.

This method was carried out on a considerably larger scale than any of the other methods to be described. Though somewhat different in design, the apparatus used was essentially the same as that described by Ruigh and Major (3). It consisted of an autoclave of about two gallon capacity equipped with an efficient agitator and charged at the outset of a run with the diethylene glycol solution of potassium hydroxide. Leading into this autoclave was a tube of small diameter through which the dichloroethyl ether could be injected. The feed rate of dichloroethyl ether was controlled by a valve and also by the pressure above the supply of this liquid in the reservoir, the variable pressure being conveniently obtained from a nitrogen cylinder. Leading into it also was another such tube through which a very small stream of ammonia was bled throughout the run. Leading from this autoclave was a reflux column of large capacity, about two inches in diameter and five feet long, in which most of the unreacted dichloroethyl ether and partially reacted β-chloroethyl vinyl ether was condensed and returned to the reaction mixture. Fairly substantial volumes of these incompletely reacted liquids escaped condensation in this reflux and for this circumstance there was provided a downward condenser from the top of the reflux column leading into a trap in which the additional condensate was retained. This condenser and trap were jacketed and held at 50° C. throughout the run. The uncondensed vapors were now led through a drying column and a downward coil condenser maintained below 0° C. into a receiver also at about 0° C. in which the divinyl ether and the volatile impurities such as acetaldehyde were accumulated. The uncondensable gases were led out doors through a flow meter so that any change in the amount of such gases was at once indicated.

In a typical run the autoclave was charged with one gallon of diethylene glycol and four pounds of 85% potassium hydroxide. During the course of three hours the theoretical quantity, 2415 Gm., of dichloroethyl ether was introduced into the reaction mixture, the temperature of the

reaction being maintained at 200–210°, after a gradual increase from 180° C. during the first forty-five minutes.

After the reaction was complete a further addition of dichloroethyl ether resulted in the production of large quantities of acetaldehyde and gaseous decomposition products, the reaction mixture having become acidic.

The crude product obtained from the final condenser prior to the generation of the large quantities of acetaldehyde above referred to consisted of 150 cc. This product lost only 6 cc. during several treatments with dilute ammonia for the removal of acetaldehyde. Considering the necessary mechanical and evaporation losses, the amount of acetaldehyde contaminating the crude yield must have been very small. From a total of 790 cc. of non-aqueous liquid reclaimed from the trap, a fraction boiling below 70° C. (mostly below 40° C.) was obtained by distillation. This fraction consisted of 110 cc. and shrunk to 105 cc. after several treatments with dilute ammonia. A total crude yield of 249 cc. (200 Gm.) or about 21% of almost pure divinyl ether was therefore obtained.[1] After drying over calcium chloride and finally over sodium, this crude product was subjected to fractional distillation through an efficient rectifying column provided with a cooling jacket to avoid superheating of the divinyl ether vapor. In this manner a purified yield of 176 Gm. or 18.2% of pure divinyl ether boiling at 28° C. was obtained, most of the shrinkage having been due to handling losses. Practically no forerunnings or residue were recovered from the distillation.

2. Second Method—Reaction between $\beta\beta'$-dichloroethyl ether and potassium hydroxide dissolved in 2-ethylhexyl alcohol.

The apparatus in which this, and the subsequent experiments were carried out consisted merely of a 500-cc., three-neck flask equipped with an efficient mercury-sealed agitator, a dropping funnel for the dropwise addition of the dichloroethyl ether, and a reflux condenser. Following the reflux condenser was a downward spiral condenser and receiver, both of which units were cooled with ice water. At the exit end of the apparatus was a gasometer in which any gaseous decomposition products could be collected by the displacement of water.

A vigorously agitated solution of 75 Gm. of 85% potassium hydroxide dissolved in 450 cc. of 2-ethyl hexyl alcohol was heated to 135° C. and the dropwise addition of 81 Gm. of dichloroethyl ether commenced. The separation of potassium chloride was immediately observed. The temperature was then raised gradually while the addition of dichloroethyl ether was continued. At about 150° C. the condensation of product was observed in the receiver. After three hours, during which the reaction temperature was maintained at 150–155° C., the addition of the dichloroethyl ether was complete. The non-aqueous portion of the condensate consisting of 35 cc. was treated with several portions of dilute ammonia, washed with water and dried with calcium chloride followed by sodium. There was no pronounced odor of acetaldehyde in the crude product and practically no shrinkage occurred during the treatment with dilute ammonia.

Fractional distillation in ordinary equipment gave the following fractions:

Fraction 1	16 cc. between 29– 40° C.
Fraction 2	4 cc. between 100–125° C.
Fraction 3	6 cc. between 160–180° C.
Residue	7 cc.
Total	33 cc.

The higher boiling fractions consisted, no doubt, of dichloroethyl ether, 2-ethyl hexyl alcohol and perhaps a small quantity of β-dichloroethyl vinyl ether. Fraction 1 upon redistillation in the equipment previously described in which divinyl ether can be distilled without superheating gave 11 cc. of divinyl ether boiling at

[1] It has been shown elsewhere, *C. A.*, 28, 5401 (1934), that pure divinyl ether will boil well above its boiling point of 28° C. unless special precautions are taken to avoid superheating, and that inconsequentially small traces of impurities arising from the reaction can elevate this boiling even up to 70° C.

27.8–28.6° C. and no liquid was discernible in the flask at the end of the distillation. Upon cooling the distillation flask 2.3 cc. of liquid condensed back into it. It is our belief that this residue was also substantially pure divinyl ether and that the only shrinkage from the yield previous to this last distillation was due to the obviously necessary mechanical losses. Calculated on a basis of the 16 cc. in hand before this step we therefore had a yield of 31–32% of theory.

3. Third Method—Reaction between $\beta\beta'$-dichloroethyl ether and sodium tertiary butylate dissolved in tertiary butyl alcohol.

Using the same apparatus and general method as was described in the previous experiment we added 34 Gm. of dichloroethyl ether to a refluxing solution of sodium tertiary butylate which had previously been prepared by dissolving 10.9 Gm. of sodium in 372 Gm. of tertiary butyl alcohol.

In this experiment the amount of condensate in the receiver was so trivial even after all of the dichloroethyl ether had been added that we used an additional 34 Gm. of this reactant. After the various purification steps had been carried out in the manner described in the previous experiment only 0.6 cc. of pure divinyl ether was obtained. The reasons for this poor result were not further investigated but it may be that the low solubility of sodium tertiary butylate in tertiary butyl alcohol as well as the low attainable refluxing temperature, *viz.*, 83–84° C., were contributing factors.

4. Fourth Method—Reaction between $\beta\beta'$-dichloroethyl ether and sodium tertiary amylate in tertiary amyl alcohol.

Dichloroethyl ether (90.8 Gm.) was added to a refluxing solution (115–120° C. oil-bath temperature) of sodium tertiary amylate prepared by dissolving 29.2 Gm. of sodium in 800 Gm. of tertiary amyl alcohol. The yield of practically pure divinyl ether, boiling point 28.3° to 29.5° C. amounted to 20 cc. or 34%.

After standing several days without any preservative this ether showed only 6–7 p. p. m. aldehyde when tested with the modified Nessler's reagent U. S. P. XI.

5. Fifth Method—Reaction between $\beta\beta'$-dichloroethyl ether and sodium tertiary hexylate in tertiary hexyl alcohol.

Dichloroethyl ether (63.3 Gm.) was added to a refluxing solution (oil-bath temperature 125–130° C.) of sodium tertiary hexylate prepared by dissolving 20.4 Gm. of sodium in 800 Gm. of tertiary hexyl alcohol. The yield of pure divinyl ether amounted to 8.5 cc. or 21%.

6. Sixth Method—Reaction between $\beta\beta'$-dichloroethyl ether and sodium 2-ethyl hexylate in 2-ethyl hexyl alcohol (octyl alcohol).

Dichloroethyl ether (45 Gm.) was added to a refluxing solution (oil-bath temperature 155–160° C.) of sodium 2-ethyl hexylate prepared by dissolving 14.5 Gm. of sodium in 256 Gm. of 2-ethyl hexyl alcohol. The yield of practically pure divinyl ether, boiling point 28–31° C. amounted to 10.5 cc. or 36%.

2.5 cc. of the divinyl ether thus prepared gave a yield of 7.6 Gm. of tetra bromo ethyl ether melting sharply at its recorded melting point, *viz.*, 64° C. This is 71% of the theoretical yield, and considering that there was an additional yield of less pure product and also many necessary losses of product it is reasonable to conclude that the divinyl ether used was practically pure.

CONCLUSIONS.

1. It has been shown that divinyl ether can be prepared in homogeneous reaction mixtures by the withdrawal of hydrogen chloride from $\beta\beta'$-dichloroethyl ether using either potassium hydroxide or sodium alcoholates when these alkaline reagents are dissolved in alcohols which do not participate in etherifications of the Williamson reaction type.

2. Suitable laboratory preparative methods for divinyl ether which involve only ordinary laboratory glass-ware and simple laboratory methods have been developed.

REFERENCES.

(1) Cretcher and Pittenger, *J. A. C. S.*, 47, 164, 1174 (1925).
(2) Hibbert, Perry and Taylor, *Ibid.*, 51, 1551 (1929).
(3) Ruigh and Major, *Ibid.*, 53, 2663 (1931).

THE HYDROLYSIS OF MENTHYL ACETATE AND ACETYLIZED PEPPERMINT OIL.*

LAWRENCE H. BALDINGER.[1]

INTRODUCTION.

In the routine examination of commercial samples of peppermint oil several questions arose concerning the kinetics of the reaction in which the acetylized oil is hydrolyzed with an alcoholic solution of potassium hydroxide. Some work has been done on the determination of the reaction velocity between menthyl acetate and potassium hydroxide (1), but apparently no investigation has been made of the reaction rate between acetylized peppermint oil and potassium hydroxide. The complexity of the constitution of peppermint oil might lead to the immediate assumption that the reaction between acetylized oil and potassium hydroxide could not be of the second order. Observations, however, showed that the reaction rates of the hydrolysis of acetylized peppermint oil and of pure menthyl acetate agree well enough to assume that the reaction of the acetylized oil is of the second order. It must be remembered that some samples of oil will show larger amounts of a constitutent, probably resinified material, which may react with potassium hydroxide to change the value of the velocity constant.

This work represents the first of a series of experiments to determine the reaction rates of the hydrolysis of acetylized peppermint oil and of menthyl acetate by potassium hydroxide in alcoholic solution at various temperatures. For the work included in this report temperatures of 25° C., 30° C. and 35° C. were used. The purpose of the menthyl acetate was to provide a standard of comparison.

REAGENTS AND EXPERIMENTAL PROCEDURE.

Peppermint Oil.—The peppermint oil used in this work was a composite sample collected during the latter part of the 1934 season. Analysis of the oil gave the following constants: Optical rotation, $-22.6_D^{27°}$; esters, 9.66%; total menthol, 50.23%. From this sample a sufficient quantity of acetylized oil was prepared according to the procedure of the U. S. P. X in the monograph for peppermint oil.

Menthyl Acetate.—Menthol, U. S. P. X, was refluxed with fused sodium acetate and an excess of acetic anhydride, C.P., for one hour. After washing with sodium carbonate T.S. to remove excess acetic anhydride, and drying over fused calcium chloride, the product was distilled under reduced pressure. The following constants were obtained: B. p. 81.5–82.5° 4 mm.; optical rotation, $-72.9_D^{27°}$.

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* Scientific Section, A. PH. A., Dallas meeting, 1936.

[1] Department of Pharmacy, University of Notre Dame, Notre Dame, Indiana.

Alcohol, Aldehyde-Free.—Ethyl alcohol, 95% by volume, was purified according to the method of the U. S. P. X.

Approximately 25 cc. of acetylized peppermint oil or menthyl acetate, accurately weighed, was placed in a 250-cc. volumetric flask and dissolved in aldehyde-free alcohol to the mark. This flask was placed in a thermostat having a temperature control sensitive to within 0.02 degree. In another volumetric flask, 250 cc. of standard alcoholic potassium hydroxide solution was placed and brought to the desired temperature in the thermostat. When both solutions had reached the same temperature, they were quickly poured into a 500-cc. flask and thoroughly mixed. A 10-cc. sample was withdrawn immediately and pipetted directly into an excess of standard acid in order to stop the reaction. The residual acid was then titrated with standard alcoholic potassium hydroxide solution, using a microburette graduated to 0.01 cc. At various intervals of time, 10-cc. portions were withdrawn from the reaction flask in the thermostat and similarly treated with acid and alkali. Phenolphthalein T.S. was used as the indicator.

THEORETICAL AND ANALYTICAL DATA.

If, in the reaction between menthyl acetate and potassium hydroxide,

$$C_{10}H_{19}OOCCH_3 + KOH \longrightarrow C_{10}H_{19}OH + KOOCCH_3$$

a and b represent the initial molar concentrations of the two reacting substances, and x the amount transformed in the interval of time t, the velocity of the reaction will be expressed by the equation,

$$\frac{dx}{dt} = k\,(a - x)(b - x)$$

which, upon integration and substitution of Briggsian logarithms, becomes

$$k = \frac{2.303}{t(a - b)} \log \frac{b(a - x)}{a(b - x)}$$

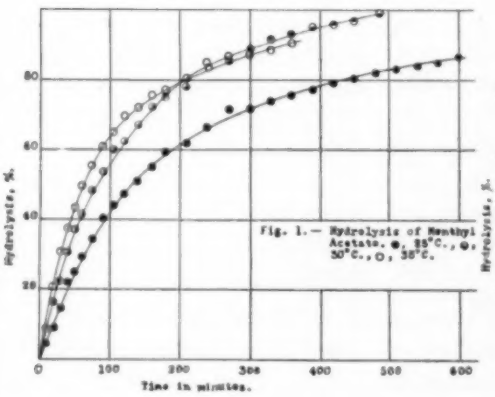

Fig. 1.— Hydrolysis of Menthyl Acetate. ●, 25°C., ⊖, 30°C., ○, 35°C.

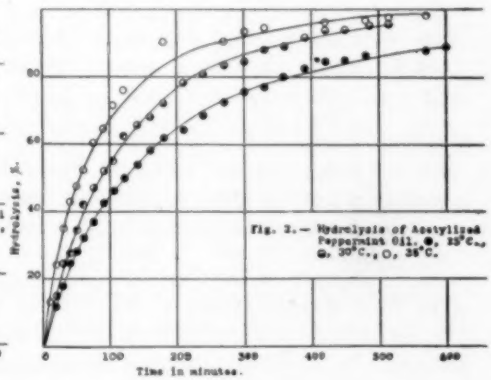

Fig. 2.— Hydrolysis of Acetylized Peppermint Oil. ●, 25°C., ⊖, 30°C., ○, 35°C.

In Tables I and II, $a - x$ is expressed as the number of cubic centimeters of 0.9744 $N/2$ sulfuric acid required to titrate 10 cc. of the reaction mixture and represents the amount of potassium hydroxide present in that volume of the mixture at the time t. The term $b - x$ is also expressed as cubic centimeters of acid of the same normality and represents the amount of menthyl acetate or acetylized peppermint oil present in 10 cc. of the reaction mixture at the time t. The term $a - b$ is expressed as the number of equivalents of potassium hydroxide present in excess in one liter of the reaction mixture. The time t is expressed in minutes.

Using the formula,

$$\text{Per cent hydrolysis} = (1 - \frac{b - x}{b})\ 100$$

the percentage of ester hydrolyzed was calculated for each experiment. See Tables I and II and Figs. 1 and 2.

TABLE I.—HYDROLYSIS OF MENTHYL ACETATE.

	25° C.			30° C.			35° C.		
t.	$a - x$.	$b - x$.	$k \cdot 10^2$.	$a - x$.	$b - x$.	$k \cdot 10^2$.	$a - x$.	$b - x$.	$k \cdot 10^2$.
0	5.593	4.693	...	5.545	3.895	...	5.515	4.705	...
40	4.562	3.662	2.572	4.340	2.690	3.893	3.745	2.935	5.377
50	4.400	3.500	2.493	4.089	2.439	4.069	3.455	2.642	5.548
60	4.235	3.335	2.412	3.928	2.278	3.974	3.170	2.357	5.808
75	3.970	3.070	2.483	3.672	2.022	4.039	2.903	2.090	5.735
90	3.710	2.810	2.595	3.448	1.798	4.119	2.655	1.842	5.822
105	3.530	2.630	2.582	3.212	1.562	4.358	2.450	1.637	5.925
120	3.380	2.480	2.551	3.114	1.464	4.163	2.290	1.477	5.909
140	3.190	2.290	2.542	2.924	1.274	4.244	2.135	1.322	5.802
160	3.010	2.110	2.564	2.725	1.074	4.487	1.960	1.147	5.971
180	2.810	1.910	2.669	2.608	0.958	4.322	1.890	1.077	5.683
210	2.710	1.810	2.479	2.458	0.808	4.499	1.740	0.927	5.683
240	2.500	1.604	2.551	2.267	0.617	4.915	1.620	0.807	5.683
270	2.240	1.340	2.859	2.222	0.572	4.626	1.460	0.647	6.150
300	2.230	1.330	2.596	2.109	0.459	4.859	1.400	0.587	6.002
Inf.	0.900	0.000	...	1.650	0.000	...	0.810	0.000	...

TABLE II.—HYDROLYSIS OF ACETYLIZED PEPPERMINT OIL.

	25° C.			30° C.			35° C.		
t.	$a - x$.	$b - x$.	$k \cdot 10^2$.	$a - x$.	$b - x$.	$k \cdot 10^2$.	$a - x$.	$b - x$.	$k \cdot 10^2$.
0	5.513	2.473	...	5.471	2.346	...	5.426	2.391	...
40	4.909	1.869	2.768	4.719	1.594	3.957	4.406	1.371	5.882
50	4.819	1.779	2.631	4.562	1.437	4.054	4.290	1.255	5.540
60	4.714	1.674	2.631	4.384	1.259	4.390	4.169	1.134	5.437
75	4.597	1.557	2.529	4.268	1.143	4.124	3.985	0.950	5.539
90	4.460	1.420	2.573	4.150	1.025	4.037	3.880	0.845	5.296
105	4.370	1.330	2.495	4.078	0.953	3.799	3.710	0.675	5.698
120	4.273	1.233	2.483	3.905	0.780	4.183	3.610	0.575	5.734
140	4.180	1.140	2.400	3.831	0.706	3.964	...	...	...
160	4.073	1.033	2.406	3.772	0.647	3.763	...	...	..
180	3.985	0.945	2.391	3.678	0.553	3.826	...	...	...
210	3.920	0.880	2.226	3.538	0.413	4.071	...	...	...
240	3.820	0.780	2.215	3.480	0.355	3.931	...	...	...
270	3.720	0.680	2.254	3.414	0.289	3.948	...	...	...
300	3.640	0.600	2.152	3.395	0.270	3.690	...	...	...
Inf.	3.040	0.000	...	3.125	0.000	...	3.035	0.000	...

CONCLUSIONS.

1. The reaction constants for the hydrolysis of menthyl acetate and of acetylized peppermint oil have been determined at 25° C., 30° C. and 35° C.

2. Until further work at different temperatures has been completed no definite conclusions can be drawn regarding the application of the van't Hoff and Arrhenius equation to the variation of the velocity constant with temperature. It has been observed in this work that the velocity of the reaction is more than doubled for a 10° rise in temperature.

REFERENCE.

(1) Nekrasova, *Arch. Pharm.*, 266, 595 (1928); through *C. A.*, 23, 474 (1929).

The author takes this opportunity to acknowledge the help of Mr. Robert F. Ervin in determining the constants in this work.

A NOTE ON THE MAGNESIA MAGMA HEAVY METALS TEST.*

BY ARTHUR OSOL AND LINWOOD F. TICE.[1]

The U. S. P. XI test for heavy metals in magnesia magma is as follows:

"To 5 cc. of Magnesia Magma, add 10 cc. of diluted hydrochloric acid and 10 cc. of distilled water, mix thoroughly, and filter if necessary. Warm the solution to 50° C., add 25 cc. of freshly prepared hydrogen sulfide T.S., and allow the mixture to stand at room temperature for ten minutes. When viewed in a Nessler tube, looking downward through the column of liquid above a white surface, the solution does not show a deeper coloration than that produced by 25 cc. of distilled water, to which 0.5 cc. of lead nitrate solution, containing 0.1599 Gm. of lead nitrate in 1000 cc. of distilled water, has been added, and treated as directed in the foregoing procedure for the Magnesia Magma."

If one follows the directions for the preparation of the standard lead sulfide sol literally he would add 0.5 cc. of lead nitrate solution to 25 cc. of distilled water, followed by 10 cc. of diluted hydrochloric acid, 10 cc. more of distilled water and, after heating to 50° C., 25 cc. of hydrogen sulfide T.S. As the volume of a standard prepared in this manner is slightly over 70 cc. the analyst, realizing that something is wrong, may simply add 25 cc. of hydrogen sulfide T.S. to a mixture of 0.5 cc. of lead nitrate solution and 25 cc. of distilled water, or he may reason that 5 cc., rather than 25 cc., of distilled water is to be mixed with the lead nitrate solution and then "treated as directed in the foregoing procedure for the Magnesia Magma," *i. e.*, adding diluted hydrochloric acid, distilled water and hydrogen sulfide T.S. In consequence of the ambiguity of the official directions at least three different methods of preparing the standard solution have been used. Briefly, the outcome has been that the test is either too stringent or too lenient, for the color produced in an acidified standard is almost imperceptible and very few magmas pass the test, while the light brown color of the non-acidified standard is sufficiently pronounced to allow practically all magmas, some of which may contain excessive quantities of heavy metals, to meet the requirements.

It may be stated here that the correct procedure in preparing the standard, according to a communication from the Chairman of the Sub-Committee on Inorganic Chemicals, is to add 0.5 cc. of lead nitrate solution to 25 cc. of distilled water and, after warming to 50° C., to add 25 cc. of hydrogen sulfide T.S.

Because of the variation in color of the sulfide sol produced by the presence of acid it was decided to investigate the effect of the free acid in the magma solution upon the accuracy of the test. The quantity of free acid in the solution remaining after the neutralization of the magma is approximately 5 cc. of diluted hydrochloric

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* Scientific Section, A. PH. A., Dallas meeting, 1936.

[1] From the Laboratories of the Philadelphia College of Pharmacy and Science.

acid. Varying quantities of lead nitrate solution were added to distilled water containing 5 cc. of diluted hydrochloric acid in a total volume of 25 cc. and, after the addition of hydrogen sulfide T.S., the color of the resulting sol was compared with that produced in an acid-free solution containing 10 parts per million of lead, *viz.*, the U. S. P. XI standard. In this way it was found that about 50 parts per million of lead could be present in the acid solution before an approximate match was obtained. It is emphasized that the comparison was an approximate one for the color produced in the acid sol was grayish whereas that of the non-acidified standard was light brown, thereby making it impossible to make an accurate comparison. By similar experiments it was found that 30 and 50 parts per million of lead, respectively, could be added to two different samples of magnesia magma before the intensity of color was judged to exceed that of the non-acidified standard.

Experiments were then made to determine whether the test could be made accurate by equalizing the acidity in the magma solution and in the standard. Colorimetric tests had shown that the reaction of the non-acidified standard sol corresponded to a p_H of about 3.2 while that of the acid magma solution was approximately 0.6. If these were equalized it is conceivable that the variation in color might be eliminated. The results of tests along this line indicated that more accurate comparisons could be made if both solutions were adjusted to the same p_H value, say 1.2, but that the color produced in a standard of this acidity was still not sufficiently pronounced to be entirely satisfactory. Reduction of acidity to p_H values above 1.2 could not be made readily because of the extensive ionization of hydrochloric acid.

At the suggestion of Joseph Rosin, of Merck and Co., experiments were made with acetic acid as a substitute for hydrochloric acid. Not only was it found that the resulting color was very pronounced and, in nearly all cases, of the same quality as that produced in the U. S. P. XI non-acidified standard but it developed that the standard sol could also be prepared with acetic acid without producing any perceptible change in its color. The desirability of adding the same reagents to the test and to the standard is obvious. Applying the modified test to twelve samples of magnesia magma it was found that only four of them passed the test whereas all of them met the requirements specified by the U. S. P. XI. However, by increasing the volume of lead nitrate in the standard to correspond to 20 parts per million of lead all of the samples but one passed the modified test. In preparing a solution of the magma 5 cc. of 36 per cent acetic acid was used to dissolve the magnesium hydroxide. The same quantity of acid was used in preparing the standard sol. Before heating to 50° C. and adding the hydrogen sulfide T.S. both solutions were diluted to 25 cc. After the addition of hydrogen sulfide the colors of the resulting sols were immediately compared because of the obscuring effect produced by the gradual formation of a precipitate resembling colloidal sulfur in the sol containing the magma. The amount of sulfur produced is not appreciable if the comparison is made within five minutes but if it is delayed to ten minutes some difficulty is occasionally experienced. It does not appear to be objectionable to make the comparison immediately after preparing the sols, this in fact being the procedure recommended by Yoe (1).

The p_H of magma-containing sols prepared with 5 cc. of 36 per cent acetic acid was approximately 4.5, whereas that of the standard sol containing the same quan-

tity of acid was 4.3. Although 5 cc. of acid constitutes an excess this quantity was used in order to minimize the buffering effect of the magnesium acetate and thereby equalize as much as possible the reactions of the two sols.

The explanation of the apparently anomalous behavior observed when hydrochloric acid is used in preparing the solution of the magma may be found in the variation of the particle size of insoluble sulfides with change in hydrogen-ion concentration. According to Thomas (2), acids are potent precipitants of colloidal sulfides, probably because such additions repress the ionization of hydrogen sulfide and drive back the hydrolysis of the metallic sulfide. If one assumes that the adsorption of hydrosulfide ion is responsible for the stabilization of sulfide sols it would follow that the stability of the sols will be decreased by an increase in hydrogen-ion concentration and vice versa, the decreased stability being evidenced by coagulation of the sulfide particles to form aggregates having, according to Rayleigh's formula (3), lower light-scattering power. Another effect which would appear to be important is the increased solubility of sulfides in acid solution due to the repression of the ionization of hydrogen sulfide by strong acids. That this effect is not of quantitative importance may be proved by calculations involving the solubility product of lead sulfide and the dissociation constant of hydrogen sulfide. Neither of the two factors enumerated above influence the sols prepared in an acetic acid medium for the ionization of this acid is insufficient to produce any significant effect.

On the basis of the experiments reported here the authors are of the opinion that the U. S. P. XI heavy metals test for magnesia magma can be improved by using 5 cc. of 36 per cent acetic acid both in dissolving the magma and in preparing the standard sol. If the change is considered desirable it will also be necessary to increase the quantity of lead present in the standard sol to, probably, 20 parts per million. This, of course, does not imply that 20 parts per million of lead will be present in magmas which just meet the requirements of the test for the latter is in fact a test for a number of heavy metals.

SUMMARY.

It has been shown that the difference in acidity between a solution of the sample being tested and the standard sol permits of the inclusion of larger quantities of heavy metals in magnesia magma than is anticipated from the lead content of the standard.

Acetic acid is demonstrated to be better suited for use in dissolving the magma.

A theoretical consideration of the variation of sensitivity of the test with acidity is presented.

REFERENCES.

(1) Yoe, J. H., "Photometric Chemical Analysis," Vol. 1, 251, 253 (1928).
(2) Thomas, A. W., "Colloid Chemistry," 185 (1934).
(3) *Ibid.*, 35.

THE POTENCY OF FIVE ADDITIONAL CARDIAC GLUCOSIDES, CALOTROPIN, α-ANTIARIN, EMICYMARIN, FOLINERIN AND SARMENTOCYMARIN.*

BY K. K. CHEN, ROBERT C. ANDERSON AND E. BROWN ROBBINS.

In a previous report (1), the comparative potency of eleven crystalline cardiac principles of plant origin was recorded.[1] Through the kindness of Doctor Rudolf Tschesche, Allgemeines Chemisches Universitäts-Laboratorium, Göttingen, Germany, three additional cardiac crystalline glucosides, α-antiarin, folinerin and sarmentocymarin, were made available to our laboratory. Calotropin was courteously supplied by Doctor Gerhard Hesse, München, Germany. Mr. Howard B. Fonda, Experimental Research Laboratories, the Burroughs Wellcome and Company, Tuckahoe, New York, was good enough to supply us a fifth compound in the present series, that is, emicymarin.

Calotropin was first crystallized with chloroform by Wieland; the glucoside and its aglucone were studied by Hesse and Reicheneder (2). α-Antiarin was isolated by Killiani (3), (4), (5), (6) from the milk sap of *Antiaris toxicaria*, and its empirical formula together with β-antiarin has been recently revised to $C_{29}H_{42}O_{11}$ by Tschesche and Haupt (7). Sarmentocymarin was first crystallized by Jacobs and Heidelberger (8) from the seeds of *Strophanthus sarmentosus*, and the structural formula of its aglucone has been elucidated by Jacobs and Heidelberger (8) and more recently by Tschesche and Bohle (9). Folinerin is a proprietary product prepared from the leaves of *Nerium oleander* (10), presumably different from oleandrin. Emicymarin is a new glucoside isolated by Lamb and Smith (11) from *Strophanthus emini*.

The five substances were subjected to similar assays and studies as previously described (1). To prepare a 0.1 per cent stock solution, sarmentocymarin was dissolved in 19 per cent of alcohol (by volume), and calotropin, α-antiarin and emicymarin, in 28.5 per cent. Folinerin is much less soluble in water, requiring 57 per cent of alcohol to effect complete solution.

The results are given in Tables I, II and III, and summarized in Table IV. It should be noted that calotropin has exactly the same potency as ouabain, as shown by the cat unit, the frog minimal systolic dose, and the cat minimal emetic dose (1). It is slightly more potent than cymarin. Folinerin has an unusually high emetic action, its minimal emetic dose in cats being only 20 per cent of the cat unit, smaller than that for any of the substances under investigation. Its effect is, however, very slow, for a majority of the cats did not vomit until more than half an hour after the injection. Two cats required a little over an hour for vomiting, and a third one, 2 hours and 7 minutes. Like digitoxin, folinerin has a very persistent action. For example, a dose equivalent to 40 per cent of the cat unit had not been completely eliminated at the end of two weeks. The protocol of that experiment may be cited here for illustration:

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* From the Lilly Research Laboratories, Indianapolis, Indiana.

[1] A typographical error should be corrected in Tables II and IV, column 3, on pages 587, 588 and 589, that is, the abbreviation "Kg." ought to be changed to "Gm." In Table IV, column 4, the minimal emetic dose in cats for digoxin should be 0.070 mg. per Kg. instead of 0.075.

11-27-1936, 8:39 A.M.—Cat No. 1528, male, weighing 1.944 Kg. was injected intravenously 0.08 mg. of folinerin per Kg. of body weight. Original pulse rate was 216 per minute.

9:12 A.M.—Cat vomited.

11-30-1936—Pulse rate was 140 per minute, slightly irregular.

12- 1-1936—Pulse rate was 188 per minute.

12- 2-1936—Pulse rate was 170 per minute.

12- 3-1936—Pulse rate was 172 per minute.

12- 4-1936—Pulse rate was 132 per minute.

12- 7-1936—Pulse rate was 148 per minute.

12- 8-1936—Pulse rate was 112 per minute. There were extrasystoles about every 10 beats.

12- 9-1936—Pulse rate varied from 126 to 184 per minute.

12-10-1936—Pulse rate was 136 per minute.

12-11-1936—Cat had lost 660 Gm. in the course of 14 days. It was sacrificed for the determination of the fatal dose, which was found to be 0.133 mg. per Kg., smaller than any observed in the series of cats for the cat unit, as shown in Table I.

TABLE I.—CAT UNITS OF CALOTROPIN, α-ANTIARIN, EMICYMARIN, FOLINERIN AND SARMENTOCYMARIN.

Drug.	Solution.	Cat Number.	Sex.	Weight, Kg.	Fatal Dose, Mg. per Kg.
Calotropin	1:100,000	1635	F	1.656	0.119
		1636	M	1.658	0.116
		1637	M	2.071	0.108
		1638	M	1.796	0.123
		1639	F	2.467	0.125
		1640	F	1.955	0.113
		1641	M	2.605	0.106
		1642	F	2.469	0.115
		1643	F	2.503	0.132
		1644	F	2.322	0.137
α-Antiarin	1:100,000	1483	M	2.280	0.135
		1484	M	2.151	0.141
		1485	F	1.949	0.109
		1486	F	1.995	0.116
		1487	F	1.907	0.137
		1488	F	2.495	0.157
		1489	M	1.970	0.123
		1490	M	1.895	0.119
		1491	M	2.016	0.147
		1492	M	1.898	0.166
		1554	M	1.821	0.159
		1555	F	2.058	0.138
		1546	F	2.532	0.097
		1547	F	2.493	0.105
		1548	F	2.109	0.130
		1549	F	2.380	0.118
		1550	M	2.480	0.143
		1551	F	2.303	0.126
		1552	F	1.933	0.104
		1553	F	1.788	0.119
Emicymarin	1:100,000	1610	F	2.628	0.132
		1611	F	2.481	0.140
		1612	M	2.339	0.194
		1613	M	1.898	0.143
		1614	M	2.344	0.166
		1615	M	2.311	0.129
		1616	F	3.140	0.141
		1617	F	1.946	0.241
		1627	F	2.074	0.251
		1628	F	2.765	0.133
Folinerin	1:100,000	1534	M	2.030	0.144
		1535	M	1.772	0.274
		1536	M	2.299	0.217
		1537	F	2.056	0.185
		1538	F	1.941	0.229
		1539	F	2.335	0.191
		1567	M	1.972	0.205
		1568	F	2.195	0.173
		1569	F	2.086	0.163
		1570	M	2.082	0.218
Sarmentocymarin	1:100,000	1502	F	2.320	0.215
		1503	M	2.600	0.225
		1504	M	2.579	0.183
		1514	M	2.695	0.234
		1515	F	2.938	0.229
		1516	F	1.882	0.182
		1517	M	2.374	0.157
		1518	F	2.170	0.309
		1519	M	2.495	0.161
		1520	F	2.548	0.212
		1544	M	1.765	0.193
		1545	M	1.956	0.166

The action of sarmentocymarin is moderately persistent since a dose equivalent to 62 per cent of the cat unit partly remained in the circulation for more than 5 days. Calotropin, α-antiarin and emicymarin are the least persistent of the five glucosides.

TABLE II.—MINIMAL SYSTOLIC DOSE OF CALOTROPIN, α-ANTIARIN, EMICYMARIN, FOLINERIN AND SARMENTOCYMARIN IN FROGS.

Drug.	Solution.	Dose, Mg. per Gm.	No. in Systolic Standstill/ No. of Frogs Used.
Calotropin	1:20,000	0.00042	0/4
		0.00046	1/4
		0.00050	6/8
		0.00054	3/4
		0.00058	4/4
α-Antiarin	1:20,000	0.00036	0/4
		0.00046	1/4
		0.00050	3/4
		0.00055	3/4
		0.00064	4/4
Folinerin	1:5,000	0.00091	0/4
		0.00109	2/8
		0.00127	3/4
		0.00145	4/4
Emicymarin	1:5,000	0.00182	1/8
		0.00205	3/4
		0.00227	3/4
		0.00273	4/4
Sarmentocymarin	1:2,000	0.00409	0/4
		0.00455	1/4
		0.00500	1/4
		0.00545	3/4
		0.00591	3/4
		0.00636	4/4

TABLE III.—MINIMAL EMETIC DOSE OF CALOTROPIN, α-ANTIARIN, EMICYMARIN, FOLINERIN AND SARMENTOCYMARIN IN CATS.

Drug.	Dose, Mg. per Kg.	No. of Cats Vomited/ No. of Cats Used.
Folinerin	0.03	0/2
	0.04	2/2
	0.05	1/1
	0.06	1/1
	0.07	1/1
Calotropin	0.05	0/2
	0.06	2/3
	0.07	3/3
	0.08	1/1
α-Antiarin	0.05	0/2
	0.06	2/2
	0.07	1/1
	0.08	2/2

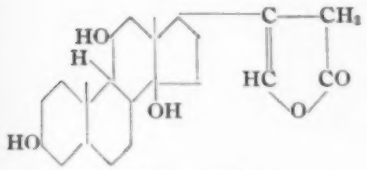
TABLE III.—*Concluded.*

Drug.	Dose, Mg. per Kg.	No. of Cats Vomited/ No. of Cats Used.
Sarmentocymarin	0.08	0/2
	0.09	2/2
	0.10	2/3
	0.11	1/1
Emicymarin	0.08	0/2
	0.09	2/2
	0.10	1/1
	0.12	1/1

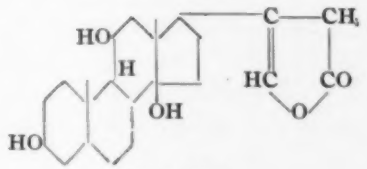
TABLE IV.—SUMMARY OF ALL RESULTS.

Drug.	Cat Unit (Mean ± Probable Error), Mg. per Kg.	Frog Minimal Systolic Dose, Mg. per Gm.	Cat Minimal Emetic Dose, Mg. per Kg.
Calotropin	0.12 ± 0.002	0.00050	0.06
α-Antiarin	0.13 ± 0.003	0.00050	0.06
Emicymarin	0.17 ± 0.010	0.00205	0.09
Folinerin	0.20 ± 0.008	0.00127	0.04
Sarmentocymarin	0.21 ± 0.008	0.00545	0.09

It may be interesting to point out that α-antiarin having the same empirical formula as β-antiarin (6), (7) and differing from the latter only by the sugar molecule (6), has a definitely lower activity than β-antiarin, the value of which was given previously (1). In the structural studies made by Tschesche and Bohle (9), sarmentogenin was shown to be an isomer of digoxigenin as follows:

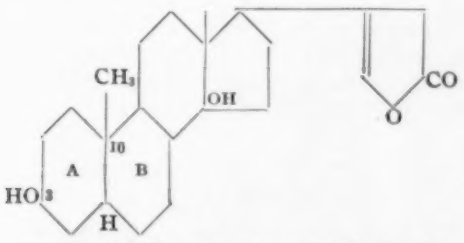


Sarmentogenin



Digoxigenin

It is therefore of more than casual interest that sarmentocymarin and digoxin have a similar potency in cats, the cat unit for the former being 0.21 mg. per Kg. and that for the latter 0.22 mg. per Kg. (1). Digoxin, $C_{41}H_{64}O_{14}$, has a larger molecule than sarmentocymarin, $C_{33}H_{46}O_8$, and thus requires a slightly larger dose. This is in contrast with digitoxin, uzarin and thevetin which have the same structural formula for their aglucone, as shown below:



Uzarigenin, Thevetigenin or Digitoxigenin

(12), (13), but which differ greatly in their cardiac activity (1). The difference is very likely due to that of the spatial arrangement of their molecules. According to Tschesche and Bohle (13), the OH group on C_3 and CH_3 group on C_{10} in uzarigenin are in *cis*-form, and its rings A and B are in *trans*-form. In thevetigenin, the OH and CH_3 groups, and rings A and B, are both in *cis*-form, while in digitoxigenin the OH and CH_3 groups are in *trans*-form and rings A and B in *cis*-form. Hesse and Reicheneder (2) showed that calotropagenin has a structural resemblance to strophanthidin. It is thus interesting to note that calotropin is only slightly more potent than cymarin, which is a conjugation product of strophanthidin and cymarose.

Regarding sarmentocymarin and digoxin in frogs, there is a considerable difference in their minimal systolic doses, the former being apparently less than half as potent as the latter. Similarly, emicymarin is more potent than folinerin according to the cat method, but is just the reverse according to the frog method. With further accumulation of data, it is hoped that an explanation for discrepancy of results between the cat method and the frog method may be forwarded at a later date.

SUMMARY.

The potency of five additional cardiac glucosides, calotropin, α-antiarin, sarmentocymarin, emicymarin and folinerin, has been carefully determined in cats and frogs.

α-Antiarin is definitely less potent than β-antiarin, Gm. for Gm.

Calotropin has exactly the same potency as ouabain.

Folinerin has a very high emetic action. Like digitoxin, it has a very slow but persistent action in the animal body.

Sarmentocymarin, which has the same structural formula for its aglucone as digoxin, possesses a similar potency as digoxin in cats.

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The authors are indebted to Messrs. Chester C. Hargreaves and William T. Winchester for their valuable assistance in making the assays in frogs.

AMERICAN MISTLETOE.*

BY F. J. DESANTIS AND E. V. LYNN.[1]

Mistletoe has been used in medicine to a limited extent since prehistoric times. Indeed, superstition has lent to its legendary powers, not only in fields other than therapy, but also for curing all sorts of ailments, a list of which would be rather long. Although opinions to-day are somewhat divided as to its merit in any one disease, it is still employed occasionally.

Only in recent times, however, have scientists found a basis for any application as a drug. Extracts of the dried plant have been reported as more or less effective agents for the reduction of high blood-pressure. Whether this property can be successfully utilized in practical therapy remains a debatable point, although some clinicians make very high claims for its remedial value.

In most chemical and pharamacological investigations on mistletoe little distinction is made between various species designated by that name. It is assumed, however, that these belong to the genus, *Viscum*, and that members of this genus share the property of reducing high blood-pressure.

The extension of this assumption to the American variety of mistletoe, *Phoradendron flavescens*, was naturally to be expected. In fact, the latter has been employed indiscriminately in medicine when mistletoe was called for. The few pharmacological studies which have been made on it are entirely inconclusive, since it has been claimed to give both a rise and a fall in blood-pressure.

On the chemical side very little has been reported about American mistletoe. Crawford, in 1911, isolated an unidentified base and concluded that it is closely related to phenylethylamine. He also stated that another more active base may probably be present and expressed the opinion that it might be acetylcholine. Hanzlik and French, in a report on physiological action, suggested that a compound like tyramine or acetylcholine is responsible. It is also interesting to note that acyl derivatives have been isolated from the European mistletoe.

The American mistletoe used in the present study was bought in the market and nothing is known of its origin. It was first submitted to a proximate analysis which gave the following results:

		Successive Extractions.	
Moisture	6.44	Pentosans	3.80
Ash	10.68	Benzin, volatile	0.08
Crude fiber	26.59	non-volatile	3.47
Tannin	3.87	Ether, volatile	0.03
Protein	15.14	non-volatile	1.62
Reducing sugars	4.48	Alcohol	16.53
Starch by acid	9.51	Water	22.46
By diastase	1.23		

In order to test for alkaloids, two pounds of the powdered material was extracted with very dilute hydrochloric acid. The solution was then made alkaline with ammonia and exhausted with ether and the ethereal solution was shaken with diluted acid. This purification process was repeated several times, finally ending

* Scientific Section, A. PH. A., Dallas meeting, 1936.

[1] Massachusetts College of Pharmacy, Boston, Mass., June 20, 1936.

with an acidified solution. This was treated with tannic acid, Mayer's reagent, picric acid and phosphotungstic acid. Since in no case was a precipitate observed, it may be concluded that ether-soluble alkaloids can be present only in minute quantity.

In spite of extensive experiments for the purpose, no crystalline glucosides could be isolated. As is well known, there is no certain method of establishing the presence or absence of such substances, since they exhibit no uniform properties as a general rule. After rendering any enzyme inert by boiling water and purifying the resulting solution by normal and basic lead acetate, the filtrate was freed from lead and concentrated. Since nothing was obtained in this way, the residue was extracted by ethyl acetate and by other immiscible solvents, but without result. It was found, however, that the aqueous solution contained notable quantities of saponin which was not strongly hemolytic.

Attempts were also made to isolate any choline derivatives. Two pounds of the powdered plant were extracted with boiling, acidified alcohol and the resulting solution was evaporated to dryness under reduced pressure. The residue was purified by exhausting with ether and again dissolved in boiling, absolute alcohol. From this solution any bases were precipitated by treating with alcoholic mercuric chloride. The dark-colored product was then suspended in water and decomposed by hydrogen sulfide. The mixture was then evaporated to dryness, taken up with water and filtered. After evaporating the liquid to a small volume, it was treated with a solution of gold chloride, giving considerable reduction to metallic gold which was removed by filtration. The solution gradually deposited yellow crystals of a compound which answered the description of choline gold chloride, but the amount was too small to purify for analysis.

SUMMARY.

1. A proximate analysis of American mistletoe was made and a table of results is given.

2. Tannin, starch pentosans and saponins are present, probably also some derivatives of choline, but alkaloids were not found.

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DRUG EXTRACTION. XII. THE EFFECT OF VARIATION IN PROPORTION OF MOISTENING LIQUID ON THE PERCOLATION OF JALAP.[1,2]

BY WILLIAM J. HUSA[3] AND PAUL FEHDER.

Experiments were carried out to determine the effect of varying the proportion of liquid used in moistening jalap on the efficiency of extraction.

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[1] Scientific Section, A. PH. A., Dallas meeting, 1936.

[2] This paper is based on part of a dissertation presented to the Graduate Council of the University of Florida by Paul Fehder, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

[3] Head Professor of Pharmacy, University of Florida.

HISTORICAL REVIEW.

Husa and Yates (1) reviewed the earlier work on the effect of variation in proportion of moistening liquid on the efficiency of percolation and carried out experiments on the percolation of powdered belladonna root which showed that there is a decrease in rate of extraction when the amount of moistening liquid is not kept down to a low proportion.

EXPERIMENTAL DATA.

Comparative percolations were carried out on 1000-Gm. portions of jalap in No. 60 powder, using varying amounts of menstruum for moistening the drug, but keeping all other factors as nearly constant as possible. The menstruum used was U. S. P. alcohol (95 per cent by volume). Four percolations were carried out, the quantities of moistening liquid used being 0, 250 cc., 500 cc. and 700 cc., respectively. A pledget of cotton was placed in the neck of each percolator and on this was placed 100 Gm. of purified sand. The drug was packed in portions. A sheet of filter paper was placed on top of the drug and covered with a layer of purified sand. Each portion of drug was macerated for 48 hours after packing.

The following portions of percolate were collected in each case: Reserve I, 400 cc., at the rate of 10 drops per minute; Reserve II, 400 cc., at the rate of 15 drops per minute; Weak Percolate, 1000 cc., at the rate of 20 drops per minute. The various fractions of percolate were assayed for resin by the N. F. VI method and for total extractive (non-volatile at 100° C.). The drug used contained 6.97 per cent resin by the N. F. VI method of assay.

By using graduated percolators it was possible to determine the volume of the packed drug. The volume of packed drug was 1400 cc. when no moistening liquid was used and 1440 cc., 1250 cc. and 1300 cc., respectively, when moistened with 250 cc., 500 cc. and 700 cc. of liquid.

TABLE I.—EFFECT OF VARIATION IN PROPORTION OF MOISTENING LIQUID.

A. Gm. of Resin in Various Portions of Percolate.

Percolates.	0.*	250 Cc.*	500 Cc.*	700 Cc.*
Reserve I (400 cc.)	45.6	57.1	50.9	36.6
Reserve II (400 cc.)	13.6	6.4	13.2	27.5
Weak Percolate (1000 cc.)	5.3	1.0	1.0	1.8
Total	64.5	64.5	65.1	65.9

B. Gm. of Total Extractive in Various Portions of Percolate.

Percolates.	0.*	250 Cc.*	500 Cc.*	700 Cc.*
Reserve I (400 cc.)	59.2	70.9	63.3	45.9
Reserve II (400 cc.)	22.5	16.6	23.8	37.3
Weak Percolate (1000 cc.)	15.5	10.4	12.4	14.7
Total	97.2	97.9	99.5	97.9

* Quantity of menstruum used in moistening 1000 Gm. of drug before packing.

DISCUSSION OF RESULTS.

The results in Table I indicate that in case of jalap there is more resin and more total extractive in the first portion of percolate when 250 cc. of moistening liquid is used than when no moistening liquid is used; as the quantity of moistening liquid increases from 250 cc. to 500 cc. and 700 cc. the first portion of percolate contains less resin and less total extractive. As far as present results go, it is concluded that jalap is extracted more rapidly if 250 cc. of moistening liquid is used for 1000 Gm. of drug than if 0 or 500 cc. or 700 cc. are used.

Husa and Yates (1) found that too much moistening liquid lowers the rate of

extraction of belladonna root and explained the results as follows: when no moistening liquid is used all of the menstruum must pass through the whole column of drug, while in case of a moistened drug each part of the moistening liquid goes through only that portion of the drug lying between it and the bottom of the percolator.

In comparing the present results on jalap with the previous results on belladonna root a difference is noted. That is, in case of jalap there is more resin in the first portion of percolate when the amount of moistening liquid is increased from 0 to 250 cc.; in case of belladonna root there was no increase in the percentage of alkaloids in the reserve portion when the amount of moistening liquid was similarly increased. In other words, the efficiency of extraction of jalap but not of belladonna root was increased by moistening with a moderate quantity of liquid. As the proportion of moistening liquid was further increased, there was a decrease in efficiency of extraction of both drugs.

The decrease in efficiency of extraction when excessive proportions of moistening liquid are used is readily understandable on the basis of the above-mentioned explanation of Husa and Yates. No definite hypothesis can be offered at this time to explain why small quantities of moistening liquid increase the efficiency of extraction of jalap but not of belladonna root; possibly the more uniform packing which is obtained with a moistened drug is more important for jalap than for belladonna root.

SUMMARY.

Percolation experiments indicate that the efficiency of extraction of jalap is greater when 250 cc. of moistening liquid is used for 1000 Gm. of drug than when the drug is packed in the dry state. As the proportion of moistening liquid is further increased there is a decrease in efficiency of extraction.

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THE STABILITY OF DIOTHANE SOLUTIONS. III.*,[1]

BY E. S. COOK AND T. H. RIDER.

It has been shown previously (1), (2) that diothane solutions when subjected to lengthy aging or sterilization undergo a slight alteration characterized by the liberation of aniline. The percentage decomposition was found to be very small—not more than 2.25% under the most stringent conditions—and is insufficient to affect the local anesthetic potency.

An extemporaneously prepared diothane solution shows no physical or chemical alteration or change in local anesthetic potency over a period of a few days if stored in pyrex containers. However, if such a solution is kept for longer periods of time, a slight change in p_H is observed together with the precipitation of the free base of diothane. We have followed the p_H changes of a number of 1% diothane solutions which were stored in pyrex bottles. The variation of p_H with aging of a typical solution is shown in Table I. The p_H determinations were made with the *quinhydrone electrode.*[2]

* Scientific Section, A. Ph. A., Dallas meeting, 1936.

[1] From the Research Laboratories of The Wm. S. Merrell Company, Cincinnati, Ohio.

[2] See page 223 for foot-note.

TABLE I.—AGING OF DIOTHANE SOLUTION IN PYREX.

Age (Months).	p_H.
Fresh	4.90
4	4.76
7	4.72
9	4.70
20	4.60

This experiment, and others not reported for lack of space, indicate that extemporaneously prepared 1% diothane solutions, when aged in pyrex, become slightly more acid and apparently tend to reach a constant p_H value. As will be pointed out later, this slight increase in acidity together with the concomitant slight precipitation of diothane free base is due to the liberation of hydrochloric acid from the salt and is not incompatible with the presence of aniline which is formed by a second type of decomposition. That the precipitate is diothane free base is shown by the fact that it redissolves upon the addition of excess acid and by melting point determinations.

It seems evident that the solution could be rendered stable by the addition of enough acid to the fresh solution to bring the p_H to approximately 4.6 by the quinhydrone electrode, or 4.8 by the glass electrode. This is, in fact, the case, and the solutions so prepared have remained without precipitation and without sensible alteration of p_H for many months. Hence, it is the practice to adjust the p_H to 4.8 by the glass electrode during the manufacture of all diothane solutions.

The changes which take place slowly on aging should occur rapidly when the solution is heated. This we have shown to be true with regard to aniline formation (1). The effects of sterilization at 100° C. on unacidified and acidified solutions in ampuls of soft glass are shown in Tables II and III. Included are figures on aniline formation obtained by our previously described method (2).

TABLE II.—STERILIZATION OF DIOTHANE SOLUTIONS IN SOFT GLASS (NO ACID ADDED).

Length of Sterilization (Hours).	p_H.	% Aniline Present.	% Decomposition.[1]
0	4.91	0	0
1	5.33	0.00067	0.30
4½	5.37	0.0025	1.13
18½	5.50	0.0050	2.25

[1] We have also employed the hydrogen electrode. The quinhydrone electrode has proved to be more rapid and to give quite reproducible results if the readings are made rapidly and the same technique is always employed. However, if diothane solutions are allowed to remain for several minutes in contact with the quinhydrone, a drifting of p_H may occur. This has led us to believe that a true equilibrium is not reached or that chemical reaction may take place between quinhydrone and diothane. Thus, while it is stressed that the quinhydrone values are reproducible, apparently they are influenced by several factors and are not an accurate measure of p_H. That this is the case is demonstrated by the fact that the glass electrode, which recently has become available to us, gives values which are 0.2 p_H unit higher than those obtained with the quinhydrone although both electrodes check on the same buffer solution. A similar behavior has been observed with procaine. It should be noted that this discrepancy does not affect the conclusions drawn in this paper since the same relative differences are found with both electrodes. Unless otherwise stated, the p_H values reported in this paper were obtained with the quinhydrone electrode.

TABLE III.—STERILIZATION OF DIOTHANE SOLUTIONS IN SOFT GLASS (ACID ADDED).

Length of Sterilization (Hours).	p_H.	% Aniline Present.	% Decomposition.[1]
0	4.71	0	0
1	4.98	0.0005	0.23
$4^1/_2$	5.00	0.0017	0.75
$18^1/_2$	5.25	0.0033	1.50

[1] The percentage decomposition in these tables is based upon one molecule of diothane yielding one molecule of aniline. Complete hydrolysis of the molecule would actually give twice this ratio and the percentage decomposition would be half the values given.

It is seen that, on sterilization in ampuls of soft glass, an *increase* in p_H takes place. Since the concentration of aniline formed is insufficient to affect the p_H, the only reasonable explanation is that the glass liberates alkali. That this is true was demonstrated by sterilizing distilled water, from which the carbon dioxide had been boiled, for various lengths of time in the same ampuls and noting the p_H changes (glass electrode) as shown in Table IV.

TABLE IV.—STERILIZATION OF DISTILLED WATER IN SOFT GLASS AT 100° C.

Length of Sterilization (Hours).	p_H.
0	7.1
1	7.5
$4^1/_2$	7.5
$18^1/_2$	7.7

The addition of acid to diothane solutions is seen not only to prevent precipitation of the free base but also to inhibit the formation of aniline to some extent.

The phenomena accompanying the aging or sterilization of diothane solutions, *viz.*, the decrease in p_H in non-alkaline containers, the precipitation of diothane free base and the formation of aniline, can be accounted for by two reactions: (1) hydrolysis of the salt (diothane hydrochloride) to give diothane free base and hydrochloric acid; (2) saponification of the free base to give piperidinopropanediol (or monophenylurethane), carbon dioxide and aniline:[1]

(1) $C_5H_{10}NCH_2CH(OCONHC_6H_5)CH_2OCONHC_6H_5.HCl \rightarrow C_5H_{10}NCH_2CH(OCONHC_6H_5)CH_2OCONHC_6H_5 + HCl$

(2) $C_5H_{10}NCH_2CH(OCONHC_6H_5)CH_2OCONHC_6H_5 + 2H_2O \rightarrow C_5H_{10}NCH_2CHOHCH_2OH + 2C_6H_5NH_2 + 2CO_2$

These reactions readily explain the beneficial effect of the addition of hydrochloric acid which tends to repress the hydrolysis by common ion effect. The presence of alkali, on the other hand, produced diothane free base by the actual neutralization of the acid portion of the salt, and we may infer that diothane solutions sterilized in pyrex ampuls would show even less decomposition than that reported. In the preparation of diothane ampuls it was found that the ordinary resistant glass ampuls of commerce contain more than a desirable amount of alkali and it was necessary to employ ampuls of special resistant glass.

[1] The primary saponification product would theoretically be phenyl carbamic acid, $C_6H_5NHCOOH$. This, of course, is incapable of existence in the free state and decomposes to carbon dioxide and aniline.

In confirmation of these reactions it may be noted that the writers have carried them out, using alcoholic potash as the saponifying agent. We have obtained aniline quantitatively and have isolated piperidinopropanediol from the reaction mixture (unpublished work).

The amount of change occurring on normal aging or sterilization, while it can be observed chemically, is too slight to alter the physiological activity beyond the experimental error of measurement. No change has been found in local anesthetic potency (3), and the aniline produced is quite insufficient to produce toxic symptoms (4). Of course, if diothane solutions are stored in non-alkali free glass, the precipitation of free base may be so great as to alter the concentration notably and thus reduce the local anesthetic potency.

This behavior is not unique to diothane: all local anesthetics of the amino ester type on which data are available show similar hydrolytic decomposition. Cocaine hydrochloride, for example, has been shown by numerous workers (5), (6), (7), (8), (9) to hydrolyze in solution with the liberation of hydrochloric acid, methyl alcohol, benzoic acid, ecgonine and the intermediate benzoyl and methyl ecgonines. This process is accompanied by a drop in p_H to 3.5–4 for a 1% solution, and by adjusting the p_H to this value minimum hydrolysis results on sterilization (7), (8). The decomposition of cocaine may be so extensive as to cause a 50% loss in anesthetic activity.

Similar hydrolysis with lowering of p_H occurs on aging or sterilization of procaine hydrochloride solutions yielding not only hydrochloric acid, *p*-aminobenzoic acid and β-diethylaminoethanol but also ammonia (5), (10). Schou and Abildgaard found 5% decomposition of procaine solution which had been aged for seven years or sterilized for 20 minutes at 120°. This decomposition was reduced to 2% when p_H was lowered to 4.35 with hydrochloric acid (0.001*N*), and this concentration of acid is recommended for the preparation of stable solutions. No significant decomposition took place when procaine solutions with this amount of acid present were sterilized for 30 minutes at 100°. The so-called alkaline solutions of procaine which are made up extemporaneously decompose rapidly, and the commercial solutions on the market claiming to be alkaline appear to have decomposed with the production of an acid p_H as indicated by the examination of several open market purchases.

Stovaine (5), (11), alypine (11), etc., also undergo similar changes.

In all of the above cases, unlike diothane, the free base is somewhat soluble in water and frequently does not precipitate upon alkalinization. There is no visible change in such solutions to indicate decomposition.

DISCUSSION.

The three individually published papers on the stability of diothane solutions complete a primary study of this problem.

All studies of the stability of diothane solutions are made unique by the almost total insolubility of diothane free base in water. This not only makes the p_H adjustment of diothane solutions a matter of considerable importance, but also helps to explain the very low concentration of degradation products which can be developed in a diothane solution, such degradation products being in most cases secondary decomposition products of anesthetic free bases.

It has been pointed out that the decomposition of diothane accompanied by the formation of aniline is not extensive enough to affect the results of biologic tests, either of toxicity or potency.

Diothane solutions are unusually stable under ordinary storage conditions and conditions of practical sterilization when compared to other anesthetics and any significant deterioration under adverse conditions is clearly marked by discoloration, precipitation or both.

Precipitation of diothane hydrochloride solution which is indicative of alkalinization and not deterioration, may be prevented or reversed by slight acidification of the solution to a true p_H of 4.8; for all practical purposes this may be attained by adding one drop of dilute hydrochloric or dilute acetic acid to each 500 cc. of one per cent solution as prepared.

SUMMARY.

1. As is typical of solutions of salts of weak bases and strong acids, diothane hydrochloride solutions are partially hydrolyzed to the free base and hydrochloric acid. On prolonged aging or heating, the traces of hydrolytic free base undergo partial degradation with the liberation of aniline. In pyrex or other highly resistant glass a lowering of p_H occurs with aging unless the original p_H was 4.8 (glass electrode) or less. If the container is of alkaline glass, the p_H shows a progressive increase with attendant precipitation of diothane free base. These changes do not involve more than a very small percentage of the diothane present and do not measurably affect the local anesthetic potency. If the solution is sufficiently alkalinized to precipitate significant quantities of the free base, the anesthetic activity obviously is lessened owing to the decrease in concentration of the solution.

2. The addition of hydrochloric acid to p_H 4.8 (glass electrode) prevents the precipitation of free base and inhibits the formation of aniline, provided the solution is stored in containers of resistant glass.

3. Changes of similar nature take place with solutions of other local anesthetics of the amino ester type.

4. Diothane solutions which for any reason have become colored or cloudy should not be used.

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SOLUTIONS FOR COLORIMETRIC STANDARDS. VIII. ARNY'S SERIES.[1]

BY C. T. KASLINE* AND M. G. MELLON.

Various uses have been found (1) for Arny's "Co-Fe-Cu" and "Co-Cro-Cu" series of colorimetric solutions. Specifications for the preparation and use of the former, or acidic, series are contained in the 1935 issue of the Pharmacopœia of the United States (9).

In view of the value which these systems have for certain work, it has seemed worth while to reëxamine their colorimetric characteristics. A more precise knowledge of their absorptive capacity is desirable from the standpoint of knowing their limitations, and of providing a basis for adapting different combinations of them to other uses.

Measurements were reported from this Laboratory several years ago (8) for the stock solutions and several dilutions of them. The data were obtained by means of a visual spectrophotometer. Unfortunately, some of the transmittancy values below 450 mμ and above 650 mμ are not reliable. The sensitivity of the eye is low in these regions and the type of instrument used in the earlier work is not capable of sufficient precision in the red and the blue portions of the spectrum. In the present work the stock solutions have been re-measured, together with the 20 mixtures of the acidic series described in the Pharmacopœia.

EXPERIMENTAL WORK.

Materials.—With the exceptions noted, the same methods of preparation of salts and solutions were followed as reported previously (8).

It may be noted that the directions given by Arny and Ring (2) for the preparation of the roseo-compound, aquo-pentammine cobaltic chloride $[Co(NH_3)_5H_2O]Cl_3$, yield instead the purpureo-compound, chloro-pentammine cobaltic chloride $[Co(NH_3)_5Cl]Cl_2$ (10). The latter compound was prepared, both according to these directions and those of Willard (12). Solutions of the two products yielded identical spectral transmission curves. The "aquo" compound, prepared according to the direction of Biltz (3), has a different hue as a solid and gives a different transmission curve immediately after dissolution, although Biltz states that the "chloro" compound dissolves in ammonia to form the "aquo" compound.

Since potassium dichromate is a primary standard, it was used to prepare the chromate solution.

Apparatus.—All the transmittancy data were obtained by means of a General Electric photoelectric spectrophotometer, a recording model of which has been described recently by Hardy (4). The method of operation and characteristics of the instrument have been described by the authors in another place (7). It is sufficient here to state that repeated checking against three glasses calibrated by the U. S. Bureau of Standards, and with lines from a mercury arc and a helium tube, led to the belief that the reliability of the wave-length values from 400mμ to 700 mμ is within 1 mμ and that of the transmittancies within one per cent. The latter values could be checked repeatedly within 0.1–0.2 per cent.

Data.—Since spectral transmission curves reveal the colorimetric characteristics of a system more quickly than tabular data, the graphical method was used, plotting per cent transmittancy as ordinates and wave-length as abscissas. All data were calculated to a basis of 10.0-mm. cell thickness by means of a special slide rule based on Bouguer's law. Figure 1 shows the results obtained for the acidic and basic series of stock solutions, and Figs. 2–6 show those for the acidic blends recommended in the Pharmacopœia. The composition of the latter solutions is given in Table I.

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[1] Abstracted from a portion of the dissertation presented by C. T. Kasline to the graduate school of Purdue University in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

* Purdue University, Lafayette, Indiana.

TABLE I.—COMPOSITION OF INORGANIC SOLUTIONS.

		$CoCl_2$.	$FeCl_3$.	$CuSO_4$.	H_2O.
Grayish	A	0.1 ml.	0.4 ml.	0.1 ml.	4.4 ml.
	B	0.3	0.9	0.3	8.5
	C	0.1	0.6	0.1	4.2
	D	0.3	0.6	0.4	3.7
Fawn	E	0.4	1.2	0.3	3.1
	F	0.3	1.2	0.0	3.5
	G	0.5	1.2	0.2	3.1
Yellow	H	0.2	1.5	0.0	3.3
	I	0.4	2.2	0.1	2.3
	J	0.4	3.5	0.1	1.0
	K	0.5	4.5	0.0	0.0
	L	0.8	3.8	0.1	0.3
Green	M	0.1	2.0	0.1	2.8
	N	0.0	4.9	0.1	0.0
	O	0.1	4.8	0.1	0.0
Pink	P	0.2	0.4	0.1	4.3
	Q	0.2	0.3	0.1	4.4
	R	0.3	0.4	0.2	4.1
	S	0.2	0.1	0.0	4.7
	T	0.5	0.5	0.4	3.6

$CoCl_2$ = 0.2500 M (1 ml. contains 0.05944 Gm. $CoCl_2.6H_2O$).
$FeCl_3$ = 0.1668 M (1 ml. contains 0.04505 Gm. $FeCl_3.6H_2O$).
$CuSO_4$ = 0.2500 M (1 ml. contains 0.06243 Gm. $CuSO_4.5H_2O$).

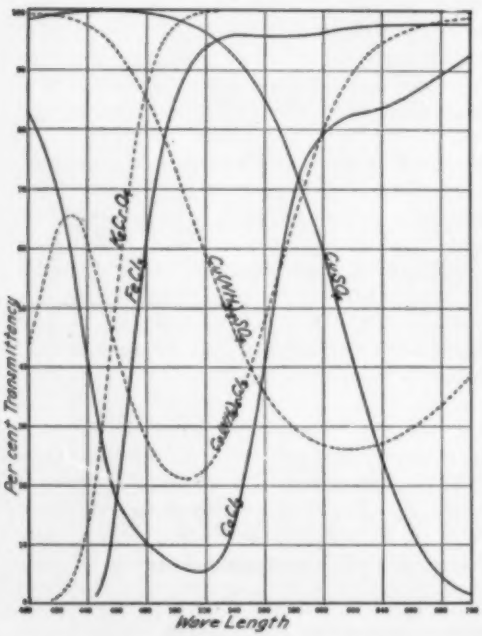

Fig. 1.—Spectral transmission curves for Arny's stock solutions.

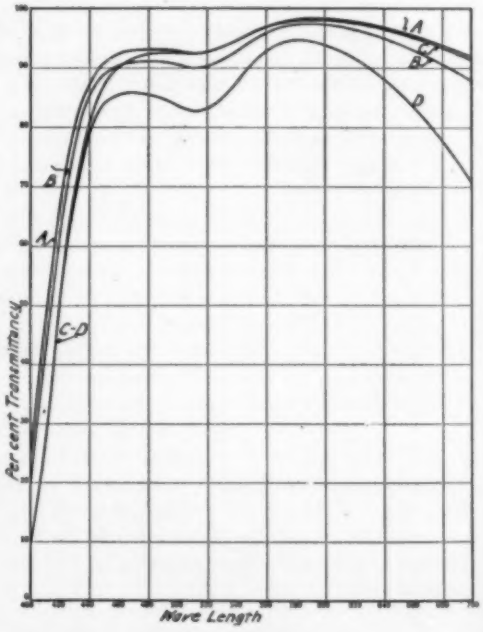

Fig. 2.—Spectral transmission curves for grayish blends.

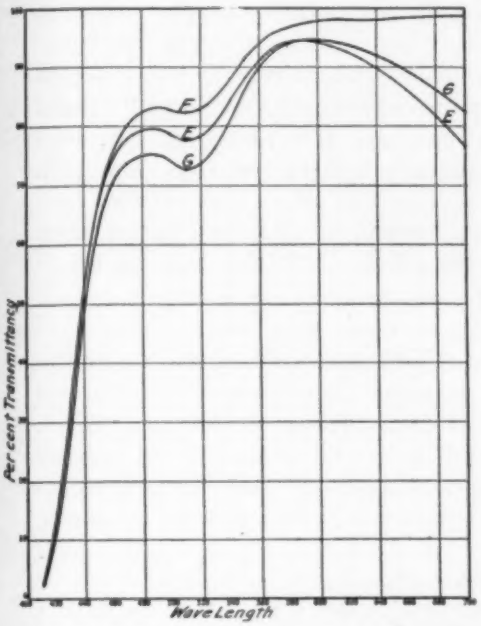

Fig. 3.—Spectral transmission curves for fawn blends.

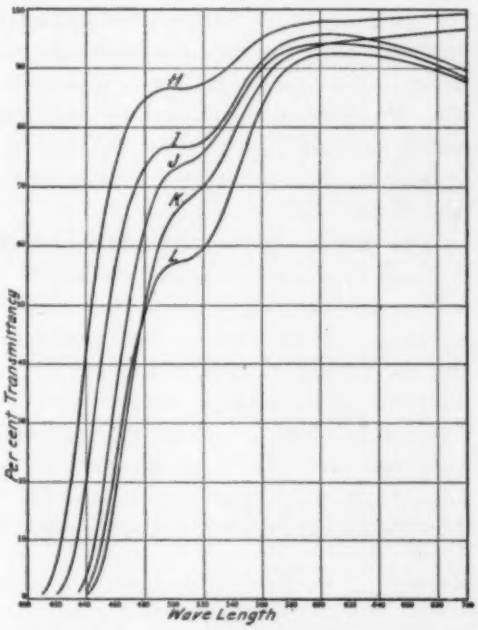

Fig. 4.—Spectral transmission curves for yellow blends.

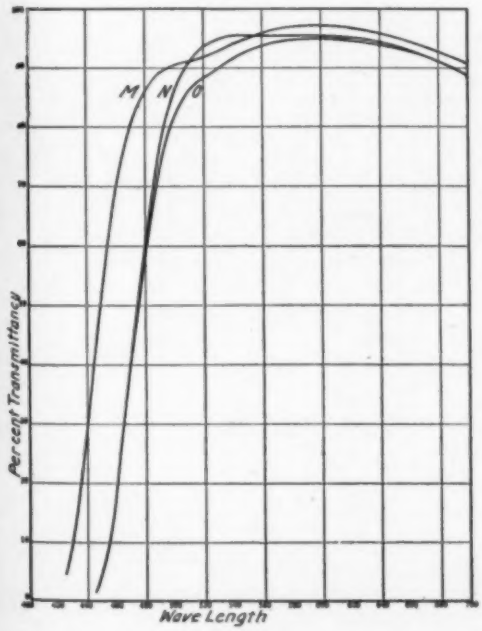

Fig. 5.—Spectral transmission curves for green blends.

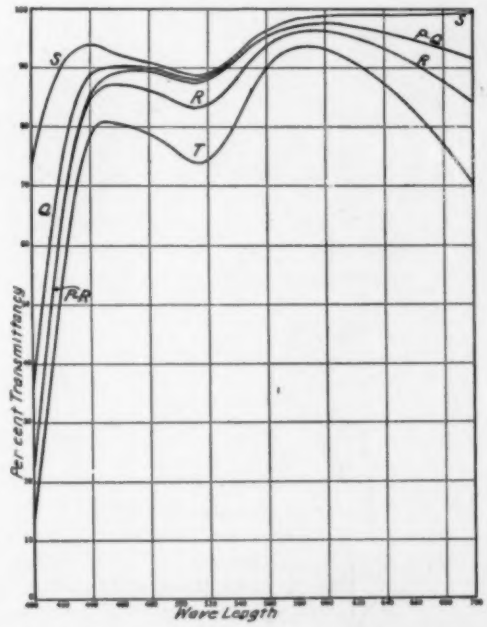

Fig. 6.—Spectral transmission curves for pink blends.

Discussion.—The curves as such require no comment. Each one represents a physical characteristic of a system just as a solubility or melting point of a compound.

In using such systems for colorimetric matching it should be kept in mind that materials matching in color under daylight may not match under artificial illumination. The curves for the two materials appearing to match may be quite different (6). But two materials having identical spectro-photometric curves will always match in color regardless of the type of illumination. It is preferable, therefore, to have an unknown which is to be matched possess a curve agreeing closely with that of the standard (11).

In view of the recommendations that have been made for employing combinations of these solutions for permanent color standards (1), the curves of Fig. 1 were used to calculate the trichromatic and monochromatic values of each stock solution. The selected ordinate method of calculation is described by Hardy (4, 5) and the values obtained are shown in Table II. An inspection of the location of the tristimulus values of these solutions in the color triangle shows that the area included by them is only a minor proportion of the total area. It is obvious, therefore, that these solutions can serve to match only a small portion of the possible colored systems. In order to extend the range one needs solutions which are redder than those of the cobalt compounds and bluer than those of the cupric compounds.

TABLE II.—COLORIMETRIC ANALYSES.

Trichromatic Values.

	Red.	Green.	Violet.
$CuSO_4$	25.3%	30.1%	44.6%
$Cu(NH_3)_4SO_4$	21.8	22.1	56.1
$CoCl_2$	43.7	30.1	26.2
$Co(NH_3)_6Cl_3$	38.3	29.1	32.6
$FeCl_3$	39.8	47.1	13.1
K_2CrO_4	36.4	42.3	21.3

Monochromatic Values.

	Brightness.	Dominant Wave-Length.	Purity.
$CuSO_4$	79.5%	487.7 mμ	22.5%
$Cu(NH_3)_4SO_4$	43.1	477	44
$CoCl_2$	40.7	700	30
$Co(NH_3)_6Cl_3$	49.8	495c	24
$FeCl_3$	92.4	570	65
K_2CrO_4	98.5	568.5	43

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VOLUMETRIC ESTIMATION OF ATABRINE DIHYDROCHLORIDE AND RIVANOL LACTATE.

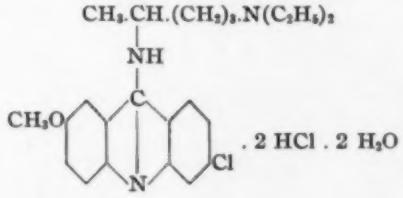
BY M. E. AUERBACH.*

The increasing application of acridine compounds in chemotherapy seems to make it advisable to acquaint investigators with a convenient method for the quantitative determination of two members of this class, namely: atabrine, which is of clinical interest in the therapy and prophylaxis of malaria; and rivanol, an internal antiseptic.

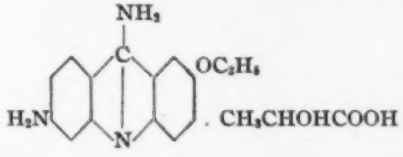
Atabrine and rivanol form difficultly soluble salts with a number of acids, *e. g.*, phosphotungstic, silicotungstic, hydriodic, salicylic, thiocyanic, ferricyanic, dichromic. Powell and Hall (1) have described a method for the determination of acriflavine which is based on the insolubility of the ferricyanic derivative. Of the atabrine and rivanol salts mentioned, however, the dichromic salt is the least soluble. Its formation has been made the basis of the method to be described, both for that reason and because it readily lends itself to a simple volumetric procedure.

FORMULAS.

Atabrine dihydrochloride is 2-chloro, 7-methoxy, 5-diethylaminopentyl amino acridine dihydrochloride. It normally occurs as the dihydrate:



Rivanol lactate is 3-ethoxy 5, 8-diamino acridine lactate:



MATERIALS USED.

The materials used were specially purified by recrystallization. The purity of the atabrine was checked by estimation of the bound HCl and water of crystallization, yielding the following figures:

Atabrine dihydrochloride (calc. from HCl)	93.20 per cent
Volatile at 100° C. (water of crystallization)	6.72 per cent

The purity of the rivanol was checked by a nitrogen determination (semi-micro Dumas):

Required for $(C_{15}H_{15}N_3O).CH_3CHOHCOOH$	12.24 per cent N
Found	12.36 per cent N

* Research Laboratories of the Winthrop Chemical Company, Inc., Rensselaer, New York.

METHOD.

0.10–0.30 Gm. are carefully weighed and introduced into a 100-cc. volumetric flask. Dissolve in 10–15 cc. water, add 10 cc. of a solution consisting of 260 Gm. sodium acetate and 280 cc. 30% acetic acid made to 1000 cc. Add 50 cc. 0.1*N* $K_2Cr_2O_7$, make up to the mark with water, mix well by transferring to a dry beaker and stirring, and filter through a dry Whatman No. 1 paper. Reject the first 15 cc. of filtrate. To 50 cc. of the subsequent filtrate in a glass-stoppered Erlenmeyer flask, add 13 cc. HCl (Sp. Gr. 1.10) and then 20 cc. 10% KI. Stopper quickly, mix by gentle swirling and let stand in the dark for two minutes. Back titrate with 0.1*N* $Na_2S_2O_3$.

50 − (cc. 0.1*N* $Na_2S_2O_3$ × 2)	=	cc. 0.1*N* $K_2Cr_2O_7$ consumed
1 cc. 0.1*N* $K_2Cr_2O_7$	=	0.00787 Gm. Atabrine dihydrochloride
	=	0.01143 Gm. Rivanol lactate.

A correction must be made to allow for the slight solubility of the precipitates, which are decomposed in acid solution, the dichromic acid portion then being back-titrated along with excess $K_2Cr_2O_7$. The following examples will make this clear:

I. *For Atabrine.*

	Weight Taken. (Reduced to Anhydrous.)	Cc. 0.1*N* $K_2Cr_2O_7$ Consumed.	Found (in Gm.).	Error (in Gm.).
A.	0.28212 Gm.	35.09	0.27616	−0.00595
B.	0.18667 Gm.	22.95	0.18061	−0.00606
C.	0.28183 Gm.	35.09	0.27616	−0.00567

The error is practically constant, allowing the final formula for percentage calculation to be written

$$\frac{(\text{Cc. } 0.1N\ K_2Cr_2O_7 \text{ consumed} \times 0.00787) + 0.006}{\text{Weight taken}} \times 100 = \text{per cent atabrine.2 HCl.}$$

II. *For Rivanol.*

	Weight Taken.	Cc. 0.1*N* $K_2Cr_2O_7$ Consumed.	Found (in Gm.).	Error (in Gm.).
A.	0.13621 Gm.	11.73	0.13407	−0.00214
B.	0.11380 Gm.	9.80	0.11201	−0.00179
C.	0.13661 Gm.	11.78	0.13464	−0.00197

Again, the error is practically constant, and the formula for calculation may be written

$$\frac{(\text{Cc. } 0.1N\ K_2Cr_2O_7 \text{ consumed} \times 0.01143) + 0.002}{\text{Weight taken}} \times 100 = \text{per cent rivanol lactic acid}$$

COMPOSITION OF ATABRINE AND RIVANOL DICHROMIC ACID SALTS.

The insoluble precipitates were washed well with water and alcohol, dried at 80° C. and then to constant weight at 100° C. Portions were then ignited to Cr_2O_3.

I.	Found, in the atabrine salt	16.86 per cent Cr
	Required for $C_{23}H_{30}N_3OCl.H_2Cr_2O_7$	16.84 per cent Cr.
II.	Found, in the rivanol salt	14.44 per cent Cr
	Required for $(C_{15}H_{15}N_3O)_2.H_2Cr_2O_7$	14.36 per cent Cr.

CONCLUSION.

A volumetric precipitation method has been described for the estimation of the acridine derivatives, atabrine dihydrochloride and rivanol lactate.

REFERENCE.

(1) Powell, A. D., and Hall, G. F., *Quart. J. Pharm. Pharmacol.*, 6, 389 (1933).

STUDIES ON THE DETERMINATION OF CAMPHOR IN CAMPHOR LINIMENT. V. IN AN ATMOSPHERE OF NITROGEN.*

BY CHARLES F. POE.[1]

Several previous communications (1) from this laboratory have shown that the U. S. P. X method for the determination of camphor in camphor liniment was not satisfactory because of the oxidation of the cottonseed oil during the heating process. Two methods which largely overcome this defect have been suggested (2): The first in which antioxidants are added before the heating; the second in which the vacuum oven is used. Of the two the vacuum oven is the more satisfactory, but unfortunately this oven is not included in the equipment of smaller laboratories.

The present communication reports the investigation of a method which makes use of the ordinary oven in which the air is replaced by nitrogen.

An air-tight oven having an inlet and outlet tube was used. A large amount of nitrogen was run through the oven at first so as to displace all the air, and then a very small amount of nitrogen was allowed to pass through during the determination. Five grams of the liniment were weighed in tin dishes. Tin dishes were used because they are deeper than the porcelain dishes which were available, and no loss was suffered by the oil creeping up the sides.

The effect of different temperatures on the heating of a sample of camphor liniment was tried. Determinations were made at 100°, 110° and 120° C. As noted in the investigation with the vacuum-oven method (2), a temperature above 120° C. was found to decompose the oil. A temperature of 110° was satisfactory and was used throughout the experiments.

A series of determinations were made by heating 5-Gm. amounts of different samples of oil in the air oven at 110° C., both with and without an atmosphere of nitrogen. The results of these determinations are listed in Table I. In an atmosphere of nitrogen, the average change in weight at the end of six hours was 0.02 per cent as compared to an average gain of 1.00 per cent when corresponding samples were heated in an air oven.

TABLE I.—CHANGE IN WEIGHT OF OILS HEATED IN ATMOSPHERES OF AIR AND NITROGEN. TEMPERATURE 110° C.

No. of Oil.	In Air. 2 Hours.	4 Hours.	6 Hours.	In Nitrogen. 2 Hours.	4 Hours.	6 Hours.
1	+0.59[a]	+0.78	+1.07	+0.04	+0.05	+0.06
2	+0.41	+0.53	+0.94	+0.07	+0.08	+0.07
3	+0.44	+0.84	+1.22	+0.09	+0.11	+0.14
4	+0.31	+0.47	+1.02	+0.04	−0.04	−0.09
5	+0.37	+0.53	+1.08	+0.10	+0.11	+0.13
6	+0.41	+0.59	+0.82	−0.08	−0.10	−0.16
7	+0.52	+0.67	+0.89	−0.06	−0.09	−0.13
8	+0.46	+0.61	+0.96	+0.08	+0.08	+0.10
Average	+0.44	+0.63	+1.00	+0.04	+0.03	+0.02

[a] Percentage gain or loss in weight.

Samples of camphor liniment, made from different lots of oil and camphor, were analyzed separately in an atmosphere of air and nitrogen, and values obtained are listed in Table II. The results when nitrogen was used were very near the theoretical values and showed better agreement than the results obtained when samples of the same liniments were heated in the air oven. The average value obtained with 20 per cent liniments for the six-hour period in an atmosphere of nitrogen was 19.89 per cent; whereas the average result in the air-oven was 19.06 per cent.

* Presented before the Scientific Section, A. PH. A., Miami meeting, 1931.

[1] University of Colorado, Boulder, Colorado.

TABLE II.—COMPARISON OF THE DETERMINATION OF CAMPHOR IN ATMOSPHERES OF AIR AND NITROGEN. 20 PER CENT LINIMENT. TEMPERATURE 110° C.

No. of Oil.	In Air. 2 Hours.	4 Hours.	6 Hours.	In Nitrogen. 2 Hours.	4 Hours.	6 Hours.
1	19.18[b]	19.36	19.08	18.16	19.78	19.92
2	19.32	19.46	18.96	18.50	19.70	19.83
3	19.10	19.46	19.07	18.62	19.88	19.90
4	18.92	19.29	19.02	18.88	19.88	19.94
5	18.66	19.36	19.07	18.56	19.75	19.88
6	19.16	19.35	19.14	18.60	19.90	19.94
7	19.34	19.28	19.04	17.92	19.82	19.84
8	19.62	19.36	19.13	17.62	19.90	19.90
Average	19.16	19.37	19.06	18.36	19.83	19.89

[b] Percentage camphor found.

In order to confirm the work given above, new samples were prepared from different samples of oils and camphor. The results which were similar to those already given are set forth in Tables III and IV.

TABLE III.—CHANGE IN WEIGHT OF OILS HEATED IN ATMOSPHERES OF AIR AND NITROGEN. TEMPERATURE 110° C.

No. of Oil.	In Air. 2 Hours.	4 Hours.	6 Hours.	In Nitrogen. 2 Hours.	4 Hours.	6 Hours.
9	+0.29[a]	+0.71	+1.09	+0.06	+0.08	+0.08
10	+0.32	+0.60	+0.88	+0.04	+0.07	+0.09
11	+0.28	+0.40	+0.63	−0.01	−0.03	−0.01
12	+0.27	+0.48	+0.68	−0.01	−0.05	−0.04
13	+0.32	+0.80	+1.03	+0.05	+0.07	+0.09
Average	+0.30	+0.60	+0.86	+0.03	+0.03	+0.04

[a] Percentage gain or loss in weight.

TABLE IV.—COMPARISON OF THE DETERMINATION OF CAMPHOR IN ATMOSPHERES OF AIR AND NITROGEN. 20 PER CENT LINIMENT. TEMPERATURE 110° C.

No. of Oil.	In Air. 2 Hours.	4 Hours.	6 Hours.	In Nitrogen. 2 Hours.	4 Hours.	6 Hours.
9	19.06[b]	19.42	18.88	18.96	19.64	19.83
10	18.19	19.40	18.75	16.69	19.68	19.82
11	18.72	19.65	19.34	19.26	19.85	19.95
12	18.04	19.50	19.20	18.68	19.80	19.88
13	18.69	19.33	19.06	18.97	19.74	19.86
Average	18.54	19.46	19.05	18.51	19.74	19.87

[b] Percentage camphor found.

Because nitrogen is somewhat expensive, the author decided to run a similar set of experiments with carbon dioxide in lieu of nitrogen. The results are presented in Tables V and VI. The U. S. P. XI directs the use of carbon dioxide (3, 4).

TABLE V.—CHANGE IN WEIGHT OF OILS HEATED IN AN ATMOSPHERE OF CARBON DIOXIDE. TEMPERATURE 110° C.

No. of Oil.	2 Hours.	4 Hours.	6 Hours.
9	+0.06[a]	+0.07	+0.11
10	+0.04	+0.06	+0.09
11	−0.04	−0.02	+0.03
12	+0.06	+0.04	+0.07
13	+0.01	+0.13	+0.16
Average	+0.03	+0.06	+0.09

[a] Percentage gain or loss in weight.

TABLE VI.—DETERMINATION OF CAMPHOR IN ATMOSPHERE OF CARBON DIOXIDE. 20 PER CENT LINIMENT. TEMPERATURE 110° C.

No. of Oil.	2 Hours.	4 Hours.	6 Hours.
9	18.76[b]	19.59	19.72
10	19.48	19.72	19.82
11	19.09	19.65	19.89
12	19.17	19.53	19.86
13	19.43	19.63	19.83
Average	19.19	19.62	19.82

[b] Percentage camphor found.

The results obtained in an atmosphere of carbon dioxide are very similar to those obtained with nitrogen, except that the results with nitrogen are somewhat closer to the theoretical percentage of camphor. Also the average gain in weight for the oils alone is somewhat lower with the nitrogen than with the carbon dioxide.

SUMMARY.

1. Experimental results are presented which show that camphor in camphor liniment may be accurately determined by heating in an atmosphere of nitrogen.

2. The substitution of an atmosphere of carbon dioxide for nitrogen gives results which approximate the accuracy of those obtained with nitrogen.

3. The results obtained with an atmosphere of nitrogen or carbon dioxide are not quite as near the theoretical values as those obtained when the vacuum oven is used.

REFERENCES.

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The 85th Annual Meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION will be held in New York City.

PHENOLPHTHALEIN STUDIES.

A Thousand Doses of Phenolphthalein: Urinalyses.*

BY BERNARD FANTUS AND J. M. DYNIEWICZ.

(AUTHORS' ABSTRACT.)

While various authorities (Sollmann (1), Bastedo (2) and others) on the subject find phenolphthalein harmless to the kidneys, there are a few reports extant that would suggest an opposite possibility.

To put this question to a crucial test, the study of a thousand medicinal doses of phenolphthalein was undertaken with special scrutiny of the effect upon the urine.

PHENOLPHTHALEIN RING TEST IN URINE.

When we perform Heller's test with an aqueous solution of phenolphthalein sodium we obtain a rather dispersed ring of turbidity through the upper layer of fluid, in dilutions down to 5:10,000.

Robert's reagent, being more sensitive, gives a turbidity in solutions of phenolphthalein sodium down to 2.5:10,000.

"Colloidal" phenolphthalein (3), which is much more soluble than the crystalline form, when added to urine to the point of saturation, gives a very definite trace of turbidity with Heller's test and a strong ring test with Robert's reagent. This is absent when crystalline phenolphthalein is used.

For differentiation between true albuminuria and this ring test due to phenolphthalein, advantage may be taken of the fact that phenolphthalein solution when heated does not become turbid even when acetic acid is added. On cooling, a turbidity may result which disappears again on heating.

We did not encounter a single instance of a false albumin test due to phenolphthalein because the total amount of phenolphthalein in the urine, both free and conjugated, never approaches the quantity necessary for the production of the phenolphthalein ring when its solution is layered over an acid reagent.

METHOD OF STUDY.

The standard methods described in textbooks were employed for the various albumin tests and in testing for sugar in the urine. The following additional tests were also employed: determination of free phenolphthalein in urine; determination of conjugated phenolphthalein in urine; determination of urine acidity by the Folin method.

VARIETIES OF PHENOLPHTHALEIN EMPLOYED.

By "white phenolphthalein" we mean the crystalline phenolphthalein described in the U. S. P. "Yellow phenolphthalein" contains about 2% of as yet unidentified colored bodies, some of which are strongly cathartic. Colloidal phenolphthalein (3) is considerably more soluble than the white phenolphthalein.

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The original publication of twenty pages has been condensed to this leaflet. The complete article, as published in the *J. A. M. A.*, 108, 439–443 (Feb. 6, 1937), with a series of tables, appears in the authors' reprints, a copy of which will be mailed on request.

OBSERVATIONS UPON NORMAL INDIVIDUALS.

The coöperation of male medical students, ranging in age from 20 to 26 years was obtained. In each a preliminary specimen of urine was secured and then the young man was given a capsule containing a medicinal dose of phenolphthalein with the direction to take it at bedtime and secure all the urine passed during the succeeding 24 hours, to mix the various specimens, to measure the total quantity, and to furnish a sample of the mixed urine for testing. Xylol was added to the specimen to present decomposition.

Six hundred and fifty observations of this kind were consistently negative on chemical as well as microscopic examination of the urinary specimens both before and after taking of phenolphthalein. It required over 10,000 tests of various kinds. In any one individual at least a week was permitted to elapse between succeeding observations.

In one case albuminuria was present in the morning specimen as well as in the 24-hour specimen, before as well as after the taking of the phenolphthalein. This is obviously an individual with a somewhat pathologic kidney and there is no evidence that the phenolphthalein increased the damage.

In two cases we found albuminuria in the 24-hour specimen, before as well as after the taking of phenolphthalein. As these men had no albuminuria in the morning specimen, we have here evidently cases of "orthostatic albuminuria." It will be noted that the albuminuria was inconstant and that it had no relation to the taking of phenolphthalein.

An occasional and very inconstant reaction to Robert's reagent was encountered in 5 cases. This was very irregular and generally occurred only once in all the various observations made in a particular individual. The fact that the other protein tests were negative, stamps these reactions as due to proteose rather than phenolphthalein.

In not one of these instances could the albuminuria or proteosuria be ascribed to the taking of the phenolphthalein.

HOSPITAL CASES.

To determine the reaction of sick individuals and especially of persons somewhat advanced in years, the kidneys of some of whom might presumably be more sensitive to injury, we studied a series of patients in the Nose and Throat service, including the Head Cancer Clinic at the Cook County Hospital, as well as of some patients in medical wards. We may summarize our findings by saying that *in all of the 150 of these patients who had no albuminuria before the administration of phenolphthalein in doses of 0.10 Gm. to 0.50 Gm. there was not a single case of albuminuria.* It required about 4500 tests to develop this conclusion.

A series of 44 patients who had albuminuria before administration of phenolphthalein was also studied and it was found that in no instance was there any evidence of increase in the albuminuria or microscopic evidence of change in the urinary sediment excepting in one patient who was under treatment for kidney stone and whose urine contained a trace of albumin before the giving of phenolphthalein. Another attack of renal colic occurred with blood and albumin in the urine. A case similar to this one has been reported in the literature and uncritically ascribed to a phenolphthalein reaction by Dr. B. Holz (4).

Interesting in connection with this study are those cases that had albuminuria before the taking of phenolphthalein and whose urinary condition improved after the dose as indicated by the reduction in the amount of albumin in the urine and the disappearance of the albumin reaction in a number of cases.

ELIMINATION OF PHENOLPHTHALEIN IN THE URINE.

Free phenolphthalein was found in only 8.5% of the medical students' urines and it was found in 21.5% of the urines of the Cook County Hospital patients. This is probably due to the following two facts:

1. The larger the dose the more frequently does free phenolphthalein appear in the urine.

2. Bacterial decomposition of the urine liberates phenolphthalein from its conjugated form.

Conjugated phenolphthalein was found in every urine specimen examined. In other words, *one can tell, by the presence or absence of conjugated phenolphthalein in the urine, whether a person has taken phenolphthalein or not.* The quantity of conjugated phenolphthalein when free phenolphthalein was also present, was always greater (with a few exceptions) than that of free phenolphthalein. *The larger the dose of phenolphthalein the greater the average amount of conjugated phenolphthalein eliminated.*

EVIDENCE FROM THE LITERATURE.

Zoltan von Vamossy (5), who discovered the cathartic action of phenolphthalein concentrated his attention on other possible effects of phenolphthalein upon the human body and was unable to discover any. Tunnicliffe (6), Mendelsohn (7), Blum (8) and Fleig (9) and many others paid a great deal of attention to the effect of the substance upon the kidney and they arrived at the conclusion that it is not only absolutely harmless to the healthy kidney but also to patients with nephritis of various kinds; and the contrast was pointed out between it and the unfavorable effect upon the kidney of a number of vegetable purgatives, such as colocynth, aloe and anthrapurpurin.

While then there is a host of witnesses corroborating the correctness of our findings, the question may be raised how it happens that some textbook writers report that phenolphthalein has produced albuminuria. A survey of the literature shows that this assertion rests upon a few sporadic case reports, Blumenthal (10), v. Jaksch (11), Fürbringer (12), all of them dating from the early days of the use of phenolphthalein, when its action was not yet understood and anything that happened after its administration was ascribed to it, and upon a report by J. L. Hydrick.

When a drug has a real tendency to produce a certain untoward manifestation the frequent use of this drug will invariably cause recurrences of the phenomenon and, the more extensively the drug is used, the more common will be the manifestation. This is illustrated by the phenolphthalein eruption of which, though it is, in point of fact, comparatively rare, we now have a definite number of cases on record.

J. L. Hydrick in 1914 (13) while a medical student, reports an unbroken series of twenty different individuals in each of whom the subject's urine showed no trace of albumin before the taking of the phenolphthalein, and in each and every one of whom positive tests for albumin were secured in the 24-hour specimen of urine ("a 24-hour specimen is important"), collected after the administration of 1- or 2-

grain doses of phenolphthalein. The finding of Hydrick's was never published excepting in abstract, because he had written in the report to the American Society of Biological Chemistry that what he had done was not for publication, but to call the attention to the fact that this was a subject which should be investigated thoroughly.

Dr. John L. Hydrick, in a personal communication of November 8, 1936, graciously states:

> "It is, of course, impossible for me to say what possible errors of technique, or what special circumstances produced the results in my experiments that were interpreted by me and by several others who saw some of my experiments, as evidence of albuminuria after taking of phenolphthalein. . . It is possible that the phenolphthalein of 1914 was not so pure as that of 1936."

CONCLUSION.

1. Medicinal doses of phenolphthalein do not produce albuminuria.

2. While free phenolphthalein is generally absent in the urine of individuals who take a small medicinal dose of phenolphthalein, conjugated phenolphthalein is always present.

3. The larger the dose, the greater the percentage of individuals passing free phenolphthalein in the urine, and the greater the amount of conjugated phenolphthalein eliminated.

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DR. FRANCISCO REDI A PIONEER IN PLANT ASH STUDIES.*

BY LYMAN F. KEBLER.[1]

INTRODUCTORY OBSERVATIONS.

During my researches in connection with the History of Federal Food and Drug Legislation, in which I have been engaged for a number of years, as time permitted, I came across a very interesting statement, in A. W. Blyth's book on "Foods," page 33 (1882), it reads:

Francesco Redi of Florence, published in 1660, on the amount of Mineral Substances in pepper, ginger, and black hellebore. He burnt 100 lbs. of each and weighed the ash: Black pepper yielded 5 lbs. 2 ozs. 4 drs. of ash, ginger 5 lbs. 3 ozs. 2 drs., while black hellebore burnt in the same quantity gave 4 lbs. of ash. These ash percentages, as we know are accurate. He treated the ash with water, and noticed that all of the salts lixiviated, had a peculiar and definite figure, which they kept although they were often resolved and afterwards congealed.

The same statement appears in Blyth's 7th, edition on "Foods," 1927.

The questions that would naturally arise in anyone's mind, in connection with the above statements, are the following:

1. Why did Redi make the determinations? 2. Why did he use 100 pounds for each plant substance? 3. How did he incinerate such large amounts? 4. Are the substances enumerated by Blyth, the only ones ashed by Redi? 5. How do Redi's ash percentages accord with modern determinations? 6. What was the purpose of lixiviating the ashes?

The reference to Redi's work was not clear, as a consequence it was several years before I came across the article in the *Philosophical Transactions*, Vol. 20, page 281 (1698), published a year after Redi's death.

FRANCISCO REDI AND HIS ENVIRONMENTS.

"Who was this pioneer, that made these ash investigations and what were his environments? Redi (1626–1697), a physician and iatro-chemist, was born a year before the distinguished Robert Boyle. He was a contemporary of Glauber, Hooke, Leeuwenhoek, Malpighi, Newton, Sydenham and John Winthrop, Jr. He lived in an era of great scientific activity. An era in which the influential Royal Society of London was organized. At a time when there were a dozen universities functioning in Italy. Alchemy had practically run its course. Iatro- or medical chemistry was to the fore. The teachings and influence of Paracelsus and his followers were still potent forces. Redi lived in Florence of Italy, a city of great influence in commerce, politics, medicine, the sciences and the arts. It was the seat of the great Florence University, founded in 1349. It was the apothecaries of Florence who requested the medical college to compile a pharmacopœia, which was done and published in 1498. Florence was at the time the name of a city and a state. This accounts in part for characterizing the 1498 pharmacopœia as the first city—state pharmacopœia. This pharmacopœia is by common accord, recognized as the first of the modern pharmacopœias."—E. KREMERS, JOUR. A. PH. A., 23, 46 (1934).

ROMANCE OF PLANT ASHES AND THEIR USES.

The fact that plants are made up in part of ashes, dates back into the remote mist of the ages. Indeed ashes have been known since the advent of the use of fire by mankind, the time of which is not recorded in history. Ashes are referred to the "Old Testament," Genesis, 18, 27, about 1898 B.C. Other references appear

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in the same publication. Some are rather interesting. Particularly those referring to the eating of ashes. "I have eaten ashes like bread," Psalms, 102, 9: "He feedeth on ashes," Isaiah, 44, 20.

An empirical knowledge of the nature of wood ashes is reflected by various writers. Jeremiah, "Old Testament," 2, 22, about 629, B.C., refers to soap, resulting from the interaction of fatty substances and alkalies. Pliny (23–79) A.D., in his immense repository, records the preparation of soap from animal fat and ashes. Pliny furthermore observes that ashes were strengthened for the making of soap, by the addition of lime. The same author notes that wood ashes were preferred to the dung of beasts. In fact the dung itself, he avers, was even burned and the ashes used in preference to the dung.

The early users of ashes knew their good effects on growing crops, but it remained for the gifted technical French chemist, Bernard Palissy (1499–1589), to point out the reason. Ashes are made up in good part of soluble salts. It was Palissy who announced the value of soluble salts in manures. This is considered the beginning of rational agricultural chemistry.[1]

Geogius Agricola (1494–1555), a noted physician-chemist, devoted a good part of his time to the study of mineralogy and metallurgy, in both of which he became a world-renowned authority. In his classic book entitled, "De re Metallica," 1556, he discusses the use of ashes derived from reeds, rushes, musk ivy, hemlock and various oaks. This interesting book has been translated into English by the former President Herbert C. Hoover and Lou H. Hoover and published in 1912.

THE RESEARCHES OF FRANCISCO REDI ON PLANT ASHES.

"Remarks Concerning Factitious Salts:[2] Drawn from a discourse written by Sen. Francisco Redi. Seignior Francisco Redi has been induced to collect divers Writings and Observations made some years past in Florence, about Vegetable Salts; which being not ready to be published, you will here receive an Extract of them, for the Satisfaction of the Curious, and Improvement of Natural Knowledge, being hereby conducted into the Manner of Extracting the Salts, their Quantity and different Figures, as likewise their Virtues and Purgative Qualities, Preparation and Circumstances."

Various sorts of flowers, fruits, herbs, woods and whatnot were burned, to make the ashes; the ashes then extracted with pure water, at the natural temperature, to make a lye, which was filtered as clear as possible. The clear lye was then put into a glass vessel, the greater part of the water evaporated, "in Balneo Marinæ," to the point that had been shown by experience to give the most satisfactory results. Redi found that five pounds of water would extract all of the soluble matter from two pounds of ashes.

"Not all herbs, nor Flowers, nor Fruits, nor Woods when they are burnt, render equally the same Quantity of Salt, but according to the Diversity of their Species, the Quantity of Salt which is drawn from the Ashes, is found different. The Seasons wherein the Plants are gathered make a Diversity, as also does the Country, whether Mountanous or Champaine or Sea-Coast or Marshy or Moist.

"All matters burnt give not the same Quantity of Ashes, but there is great Diversity which you may see by the following Proofs, the great Part in the year 1660, in the Time of the Most Serene Great Duke Ferdinand II, of Glorious Memory."

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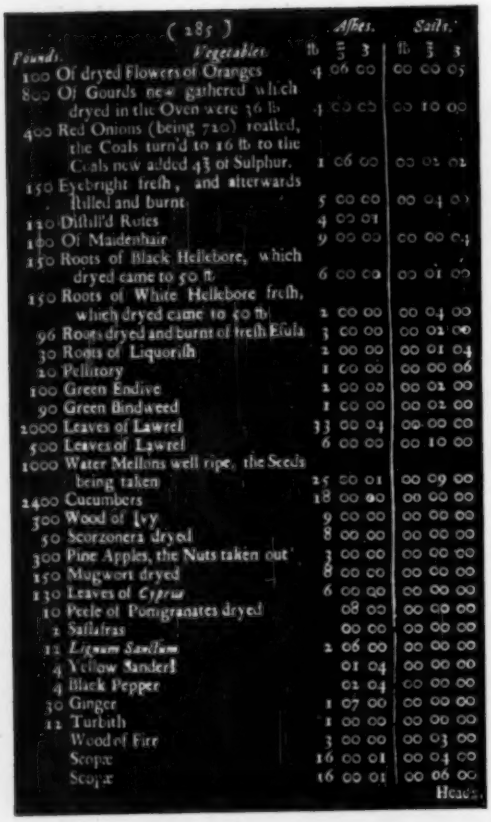
[1] "History of Chemistry," Ernst von Meyer, translated by George McGown, page 96 (1906).

[2] *Phil. Trans.*, 20, 281 (1698).



(185)

Pounds.	Vegetables.	Ashes. lb	℥	ʒ	Salts. lb	℥	ʒ
100	Of dryed Flowers of Oranges	4	06	00	00	00	05
800	Of Gourds new gathered which dryed in the Oven were 36 lb	4	00	00	00	10	00
400	Red Onions (being 720) roasted, the Coals turn'd to 16 lb to the Coals now added 4½ of Sulphur.	1	06	00	00	01	02
150	Eyebright fresh, and afterwards ſtilled and burnt	5	00	00	00	04	00
120	Diſtill'd Roſes	4	00	01			
100	Of Maidenhair	9	00	00	00	00	04
150	Roots of Black Hellebore, which dryed came to 50 lb	6	00	00	00	01	00
150	Roots of White Hellebore freſh, which dryed came to 40 lb	2	00	00	00	04	00
96	Roots dryed and burnt of freſh Ebula	3	00	00	00	02	00
30	Roots of Liquoriſh	2	00	00	00	01	04
20	Pellitory	1	00	00	00	00	06
100	Green Endive	2	00	00	00	02	00
90	Green Bindweed	1	00	00	00	02	00
2000	Leaves of Lawrel	33	00	04	00	00	00
500	Leaves of Lawrel	6	00	00	00	10	00
1000	Water Mellons well ripe, the Seeds being taken	25	00	01	00	09	00
2400	Cucumbers	18	00	00	00	00	00
300	Wood of Ivy	9	00	00	00	00	00
50	Scorzonera dryed	8	00	00	00	00	00
300	Pine Apples, the Nuts taken out	3	00	00	00	00	00
150	Mugwort dryed	8	00	00	00	00	00
130	Leaves of *Cyprus*	6	00	00	00	00	00
10	Peele of Pomgranates dryed		08	00	00	00	00
2	Saſſafras		00	00	00	00	00
12	*Lignum Santlum*	2	06	00	00	00	00
4	Yellow Sanders		01	04	00	00	00
4	Black Pepper		02	04	00	00	00
30	Ginger	1	07	00	00	00	00
12	Turbith	1	00	00	00	00	00
	Wood of Fire	3	00	00	00	03	00
	Scopæ	16	00	01	00	04	00
	Scopæ	16	00	01	00	06	00

Heads

Fig. 1.—Redi's tabulated results of plant ashes and the soluble salts contained therein.

(186)

Heads of Old Garlick 32 lb were dryed in a Furnace and burnt, from the Aſhes there was hardly any Salt to be gathered.

Thirty Pounds of Wheat-Flower burnt in a Furnace with a little Sulphur, and burnt a new in a Potter's Oven, give 8 ℥ of very black Aſhes, the which being Baked again for Eight Days continually in a Brick Furnace, after the Lye was made, there could not be a Grain of Salt drawn. The like happen'd in 10 ℥ of Aſhes drawn from a Stare and a half of Bran, burnt firſt in the Furnace with Sulphur, and afterwards baked in a Potter's Oven, and in one of Bricks.

Fig. 2.—Soluble salts in the ashes of garlic, wheat and bran.

16. All the Salts whatever drawn from the Aſhes of Vegetables, taken by the Mouth, ſays he, have a Purging Faculty, and a great Meaſure more than what by ſome is believed in common Salt, which taken by the Mouth has little or none at all, or if it have any betwixt that of common Salt and Vegetables, the Proportion is but as Two to Eight.

17. This Solutive Faculty is of equal Energy in all the Salts in ſuch Manner that the Salt of Sumack, Peeles of Pomgranates, Mirtle Berries, or Maſtick Purges as much as the Salt of Rubarb, Sena Turbith, Mechoacan, and all other like purgative Drugs.

18. The Doſe to be uſed is the ſame in all the Salts, to wit, from Two Drachms and an half to half an Ounce, diſſolved in Six Ounces of common Water; and Broth, he has obſerved by infinite Experiments, that half an Ounce uſes to Purge Three Pounds and a half, or Four, or thereabouts, of Matter more or leſs, according to the Complexions, and according to the Fulneſs of the Bodies.

19. In Purging he has found no difference betwixt theſe Salts that have ſharp Points, and thoſe that are obtuſe and blunt or cubical; he has made Proof very often in divers Perſons, cauſing the like cubical Stones of Cucum-

(187)

bers, Ginger, Colewort, and of Liquoriſh to be picked out, and he has ſeen that they have worked with the ſame Energy as the moſt acute Hexagone Stones of the Salt of Pepper, of Carnation Roſes, of Mechoacan, of Coleworts, of Cucumbers, &c.

20. From the aforeſaid Obſervations, tho' you cannot eſtabliſh a certain Rule, you may nevertheleſs conjecture, not without ſome Reaſon, *Firſt*, That the Salt drawn from the Aſhes of Herbs, Flowers, and of Fruits, &c. do not conſerve the Virtue, and that Faculty which Phyſicians believe the Herbs, Flowers, Fruits, &c. are endowed with. *Secondly*, You may very near be certain of the Proportion of Aſhes riſing from each Species of Vegetables, and of the Quantity of Salt which is afterward to be drawn from them; and it will not be ungrateful to the Reader that I put here the Differences by me computed (of the Aſhes, after the rate of 100 Pounds of Vegetables, and of the Salts after the Rate of One Pound of Aſhes) and depoſed according to the Order of the Exceſſes.

Fig. 3.—The purging or laxative properties of certain plants are not due to the soluble salts extracted from the ashes.

These interesting observations, on the ash content of plants, varying with the species, the condition under which they are grown, and the time of collection, made over two centuries ago, are the earliest recorded and hold good to this very day.

The information is now available to answer the questions propounded in connection with the statement quoted from Blyth.

A Table of the Ashes which 100 lb *give.*

	lb	℥	ʒ	℈	gr.
Red Onions	00	04	04	00	00
Gourds	00	06	00	00	00
Cucumbers	00	09	00	00	00
Pine Nut-Shells	01	00	00	00	00
Yellow Sanders	01	00	04	00	00
Bindweeds	01	01	02	02	00
Laurel Leaves	01	02	00	00	00
Roots of White Hellebore	01	04	00	00	00
Other Leaves of Laurel	01	07	04	02	10
Endive	02	00	00	00	00
Wheat Flower	02	02	05	01	00
Water Melons	02	06	00	00	00
Ivy	03	00	00	00	00
Roots of Efula	03	01	04	00	00
Saſſafras	03	01	04	00	00
Eyebright	03	04	00	00	00
Diſtill'd Roſes	03	04	00	00	00
Roots of Black Hellebore	04	00	00	00	00
Orange Flowers	04	06	00	00	00
Leaves of Cyprus	04	07	03	05	00
Pellitory	05	00	00	00	00
Black Pepper	05	02	04	00	00
Ginger	05	03	01	02	00
Mugwort	05	04	00	00	00
Pomgranate Bark	06	08	00	00	00
Roots of Liquorith	06	08	00	00	00
Turbith	08	04	00	00	00
Maiden-Hair diſtill'd	09	00	00	00	00
Scorzonera	16	00	00	00	00
Lignum Sanctum	20	10	00	00	00

Fig. 4.—See title, top of plate. Second part 4 top of next column.

A Table of the Salts which are extracted from One Pound of Aſhes.

	lb	℥	ʒ	℈	gr.
Maiden-Hair	00	00	00	01	08
Roots of Black Hellebore	00	00	00	04	00
Orange Flowers	00	00	01	00	08
Lawrel Leas	00	00	03	01	22
Root of Efula					
Roots of Liquorith	00	00	06	00	00
Pellitory	00	00	06	00	00
Water Melons	00	00	06	01	11
Red Onions	00	00	07	01	00
Endive	00	01	00	00	00
Fitr	00	01	00	00	00
Roots of White Hellebore	00	01	00	00	00

Scopæ

Fig. 4.—Second part. See legend at top.

(289)

	lb	℥	ʒ	℈	gr.
Scopæ	00	01	00	00	00
Another	00	01	01	00	00
Eye-bright	00	01	01	01	09
Other Leaves of Lawrel	00	01	05	01	06
Bindweed	00	02	00	00	00
Gourds	00	02	04	00	00
Roſes	00	03	00	00	00

In this Table you ſee ſome Variation in the ſame Species of Vegetables, the which do not give always the ſame Quantity of Aſhes and Salt, and that which is conſiderable, ſome Vegetables, inſipid and cold, as Endive, Pompion, and Roſes, have given much more Salt than others of a ſtronger Savour, apertive, and inciſive, as the Onions, Hellebore, Lawrel, Maiden-Hair, and the Garlick which is ſo ſtrong, gives none at all: But it may perchance be ſaid, that in theſe there is a greater Quantity of Volatile Salt.

Fig. 5.—See explanation in plate.

1. Why did Redi make the determinations? Redi's objects were first to ascertain the degree of purgation present in the soluble salts of the ashes of the various plants tested; second, whether the laxative nature of the plants was due to the salts lixiviated from the ashes or not; and third, were the salts extracted from the various ashes the same, similar or different. It is quite apparent that the percentages of the ashes and the salts in the ashes recorded were largely incidental.

2. Why did Redi use 100 pounds for each plant substance ashed? The prime purpose for using large amounts was, apparently, to obtain sufficient ash, to make enough soluble salts, to enable him to test their physiological effects. A glance at the table shows that the amounts varied from 2 pounds in the case of sassafras to 2400 pounds in the case of cucumbers. Redi ashed 4 pounds of black pepper, 30 pounds of ginger and 150 pounds in the case of hellebore. From the results obtained, Redi did calculate the amount of ash, that would be present in 100 pounds, of thirty different products, but this is quite different from saying that Redi "burnt 100 pounds of each and weighed the ash."

3. How did he incinerate such large amounts? This is not clearly set forth in the article. Reference is made to the drying and burning and baking in a brick furnace, and in a potter's oven, but this is not as conclusive as it might be. One must take into consideration the large amounts ashed and the state of the developments of the arts.

4. Are the substances enumerated by Blyth, the only ones ashed by Redi? The answer is clearly no, but they probably served Blyth's purpose.

5. How do Redi's ash percentages agree with modern determinations? Blyth says: "These ash percentages as we know are accurate." It is well known that the ash content of the same part or parts of plants vary considerably, depending on a number of circumstances. Redi calls attention to several of them. The characters used in the article show that the author employed the apothecary system of weights in making his determinations, excepting the term "Stare" used in connection with the ashing of bran. This unit according to the "New English Dictionary" (Murray), appears to represent 220 pounds. The Doctor's data give the following percentages: Black hellebore 4%, black pepper 5.21% and ginger 5.27%. Modern determinations record the following: black hellebore 6.6%, black pepper 3.5–7% and ginger 5.25–7.5%. The latter percentages show that Redi's results agree well with the average of recent date. It may further be said, that his results, for some of the other plant substance ashed, are in good accord with the findings of modern investigators, in spite of the apparently crude method employed by him.

6. What was the purpose of lixiviating the ashes? The amounts of the water-soluble salts, are given in tabulated form, but it is quite evident that the chief purposes were, to ascertain the medicinal and crystalline natures of the salts extracted.

CONCLUDING OBSERVATIONS.

Redi's report on the study of ashes, stands by itself, in this field. It is one of the most interesting articles that it has been my privilege to study. To my mind it is a real classic. No important investigation, of any kind, on plant ashes, is reported for more than two centuries, following the studies of Redi in 1660. From this it must not be assumed that interest in plant ashes had ceased all this time. On the contrary it is reported that pot-ashes were made in Virginia and exported as early as 1608. In 1661, the exportation of potash, from the American Colonies, to any country, but England was prohibited by Parliament. The American forests continued to be burned, the ashes converted into pot and pearl ashes and exported for many years, thereafter.

It may be of interest to note that Samuel W. Johnson, professor of analytical and agricultural chemistry of Yale, compiled the trustworthy analytical data of the ashes of agricultural plants and products thereof, in print in 1867 and published the results in his book, entitled, "How Crops Grow," in 1868. The data are based largely on the work of Emil Wolff and his associates. Redi's work dealt largely with medicinal problems and was not referred to by any of the above workers.

GILES FIRMIN, SENIOR.[1]

BY WILL T. BRADLEY.[2]

In the fall of 1633, hands were imposed upon Giles Firmin, Senior, newly come from Sudbury in England to the colony settled about Massachusetts Bay, and he was thus made a deacon of the Boston church. A very godly man, upwards of forty years old, with some experience of public life in his youth, he proved a valued member of the community, was soon made a selectman, and served conscientiously; but during the hot months of the following summer he sickened, and by the time it was fall again he was dead. Very little else up to now has been known about him.

[1] Section on Historical Pharmacy, A. PH. A., Dallas meeting, 1936.

[2] Instructor in English and French, Massachusetts College of Pharmacy.

For us he would have no more interest than have most of the thousands who came to the New World speedily to perish were it not for the fact that in his history of the early colony Governor John Winthrop says that Deacon Giles Firmin was not only a godly man but also an apothecary.

I say very little else has been known about him. Some investigators have casually confused him with another Firmin, who came over in the fleet with Winthrop in 1630; but this Firmin was named John;[1] he settled at Watertown, lost his shack by fire on November 11, 1630,[2] and on May 18, 1631, took the oath of allegiance without which none were regarded as freemen, or members of the body politic;[3] he may have been the same John who in 1638 was a selectman and deacon;[4] he was no doubt a cousin or near relative of our Giles Firmin. Other investigators have been misled by the fact that our apothecary had a son by the same name,[5] who came for a brief visit to Boston in 1632, returned here again to practice medicine, mostly in Ipswich, from 1637 to 1644, delivered the first anatomical lectures to students in this country, perhaps at Harvard College,[6] and then went back to England, where he entered the ministry and enjoyed a life full of preaching, writing, and controversy until his death at a tardy age in 1697.

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[1] James Savage, "A Genealogical Dictionary of the First Settlers of New England" (Boston: Little, Brown and Company, 1860).

[2] John Winthrop, "The History of New England from 1630 to 1649," edited by James Savage (Boston: Little, Brown and Company, 1853), page 38.

[3] "New England Historical and Genealogical Register," Vol. 3 (1849), page 91.

[4] Savage, "Gen. Dict." According to the "N. E. Hist. and Gen. Reg.," Vol. 14 (1860), page 329, a note of the names and ages of passengers sailing in the *Elizabeth* of Ipswich (England), Mr. William Andrews, Captain, bound for New England the last of April 1634, includes the name of John Firmin, aged 46. Savage thought that perhaps this was the same John who came first in 1630, but this is unlikely, for he would have had to return to England, and at least two John Firmins took the oath of a freeman in Boston. The first was probably the selectman in 1638, for according to the "N. E. Hist. and Gen. Reg.," Vol. 3 (1849), page 187, the second John Firmin did not take the oath until May 13, 1640.

[5] For the best brief discussion of the son see John Ward Dean, "A Brief Memoir of Rev. Giles Firmin, one of the Ejected Ministers of 1662" (Boston: David Clapp and Sons, 1866), reprinted from the "N. E. Hist. and Gen. Reg." for January 1866, and some further remarks by the same author in the "Reg.," Vol. 25 (1871), page 52.

[6] A letter written in 1647 by the Apostle Eliot, addressed to the minister of Cambridge, Massachusetts, contains an interesting remark: after pleading for a school for teaching medicine here, equipped with "anatomies," or skeletons, and imported "vegetables vertuous in the way of Physick," he adds, "We never had but one Anatomy in the countrey, which Mr. Giles Firman now in England, did make and read upon very well. . . ." Before the founding of Boston, a man named Lambert Wilson had been engaged by the New England Company not only to serve as a chirurgeon in the colony but "to educate & instruct in his Art one or more youths." Eliot's letter apparently revived interest in the subject, for during a session of the General Court in 1647 it was decided that "we conceive it very necessary yt such as studies phisick, or chirurgery, may have the liberty to read anotomy & to anotomize once in foure yeares some malefactor in case there be such as the Courte shall alow of;" but nothing seems to have been done further, except the granting of limited permission to physicians and their students to dissect the bodies of criminals, and the Harvard Medical School was not established until after the Revolution. Where Giles Firmin got his bones and where he read upon them are not known: that these first medical lectures in America were delivered at Harvard is only a guess. See "Memorial History of Boston," edited by Justin Winsor (Boston: James R. Osgood and Company, 1881), Volume 4, Chapter 10 ("Medicine in Boston" by Samuel A. Green, M.D.), pages 529–530; also Oliver Wendell Holmes, "Medical Essays."

I have searched scores of available records that might tell us more about Giles, Senior, since if we grant the desirability of knowing as much as we can about the first pharmacist to settle and die in New England, every new fact we can learn, however slim or trivial, is precious. Though the definite facts still remain few indeed, our knowledge of contemporary events will allow us to deduce others not shown in the records, and the man will take shape and substance, much as a prehistoric creature emerges though we begin with nothing but an eager imagination and a broken tooth.

The earliest Firmin of whom we have any trace lived at Bury St. Edmund's, county Suffolk, in the reign of Henry VIII.[1] The will[2] of his widow, proved on December 18, 1540, left to her two sons and daughter houses and possessions that suggest something better than moderate means. Naturally the family at that time was Roman Catholic.[3] During the next century a succession of baptisms, sales, marriages, and wills reveals the Firmin family spreading in a number of fairly well-defined branches through the counties of Suffolk and Essex, northward and eastward of London.

The will[4] of "Giles Firmyn of Stoke Nayland" (born before 1570, died 1597) names a wife Katherine, sons Josias, John, *Giles*, Henry, and daughters Frances, Anne, and Sara. That this son Giles was our apothecary is quite possible, for there is no record of our man's birth in Sudbury,[5] and he may have gone down in his youth to serve his apprenticeship in the larger town. These Firmins of Stoke Nayland appear to have belonged to a humble branch of the family: several were tanners, others were farmers, and the daughter of one (a "Gyles" who died in 1584, the oldest Giles on record) married a blacksmith.[6]

But the will[7] of "Richard Fyrmyn, Gentleman, of Sudbury," dated November 2, 1614, and proved January 9, 1615, is more promising. He had been an alderman,[8] and his bequest of four acres of lease land in Windmill Field to the poor of the town (income to be distributed each Christmas, amounting to eight pounds in 1902) makes him still remembered there.[9] Among liberal bequests that prove him for those times wealthy, he left to *sons Giles and Thomas and two daughters of his deceased brother Thomas* five pounds each, and to the boys and their heirs, after the

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[1] Christian name unknown. Since his married daughter was probably born before 1517, he must have been born before 1496; he died before 1538, when his widow made out her will.

[2] Quoted in "Wills and Inventories from the Registers of the Commissary of Bury St. Edmund's and the Archdeacon of Sudbury," edited by Samuel Tymms (London: printed for the Camden Society, 1850), pages 135–137. Among her bequests were several pots and caldrons and "1 brazen mortar with the pestle."

[3] She left "to the high alter of the said church, for my tithes and oblations negligently forgotten, in discharging of my conscience" six shillings eight pence, and to "Signior Wylliam Norman, priest, to pray for my soul, my friends' souls, and all Christian souls" eight marks sterling.

[4] Quoted in James A. Emmerton and Henry F. Waters, "Gleanings from English Records about New England Families" (Salem: Salem Press, 1880), from "Hist. Coll. Essex Inst.," Vol. 17, No. 1, page 34.

[5] "N. E. Hist. and Gen. Reg.," Vol. 25 (1871), page 52.

[6] Emmerton and Waters, "Gleanings," page 36.

[7] Quoted in Emmerton and Waters, *Ibid.*, pages 36–37.

[8] Rev. Charles Badham, "The History and Antiquities of All Saints Church, Sudbury" (London: Hatchard and Son, Piccadilly, 1852), page 174.

[9] "N. E. Hist. and Gen. Reg.," Vol. 56 (1902), page 183.

death of his wife, a "close or pasture next adjoining Brackets Bridge, said land to be sold by Giles and Thomas to John Firmin, Kinsman, for 40 pounds." The terms of these bequests seem to indicate that nephews Giles and Thomas had come of age in 1614, and they would therefore have been born before 1593.

Now, here is a Giles Firmin who may most plausibly be identified with our apothecary, who must have been born before 1593, since his son, Giles, Junior, was born in 1614 or 1615.[1] The evidence is not conclusive, but it is easy to understand how the nephew of Richard Firmin, gentleman and public benefactor, could have achieved the distinction of alderman or councilor in the town of Sudbury—a distinction that our Giles, as will be seen, almost certainly did achieve.

From what evidence we have, then, we may believe that our Giles was born in or near Sudbury of this more prosperous branch of the family; that his father, Thomas, and his mother were both dead in 1614; that he had a brother Thomas[2] and two sisters; that his near relatives (mentioned in Uncle Richard's will) were these: an uncle William Firmyn (deceased), who had three sons; an uncle Nicholas Firmyn, who had three daughters; an uncle John Firmyn (deceased), who had two daughters; an uncle Roger Firmyn, who had a son Benjamin; and an aunt Joan (Firmyn) Chaplyn (deceased), who had four daughters; and that other kinsmen included Josias Firmyn, tanner, of Nayland;[3] John Firmyn, clerk, of Foxearth, and his son John, also a clerk; Richard Cooke of Great Henny, in Essex; Roger Cooke, of Brently; John Firmyn, shoemaker, of Hadley; Clemence (Firmyn) Cooke, sister of kinsman John Firmyn; and cousins Henry and John Cooke.

In the boyhood and youth of Giles, the lonely, aging Elizabeth, under the control of ministers who had put her there, was maintaining the glittering tyranny of her father's throne. The era held rare suspense for youngsters of that generation: economically, politically, philosophically, horizons were broadening—a polite way of saying that old standards were crumbling, disagreements were rising on matters of common sense; judgments based upon long and successful experience

[1] Dean, "A Brief Memoir," page 5.

[2] In 1635 a Thomas Firman went with his wife Sarah to settle in Ipswich, Massachusetts, where Giles, Junior, went to practice medicine in 1638. He was a successful merchant and much interested in acquiring real estate, for from 1638 to 1647 we find him buying many houses and lots. In 1639 he received a license to operate an ordinary, or inn, and by 1646 he was recognized as a leading citizen of the town. He was undoubtedly a relative and may have been the brother of our apothecary. He and Giles, Junior, took the oath of a freeman together on May 22, 1639. He died in 1648. See Rev. Thomas Franklin Waters, "Ipswich in the Massachusetts Bay Colony," Vol. 1, pages 13, 21, 351, 384, 389, 445, 491, and Vol. 2, pages 66, 721; also "N. E. Hist. and Gen. Reg.," Vol. 3 (1849), page 156 and Vol. 6 (1852), page 253; also Savage, "Biog. Dict."

[3] Quite possibly the son Josias, mentioned in the will of "Giles Firmyn of Stoke Naland," whose brother Giles, we have seen, *may* have been our apothecary. His will, proved in November 1638, is quoted in Emmerton and Waters, "Gleanings," page 38. In it he names his eldest son Josias and his youngest son Gyles. The ship-money tax imposed by Charles I put heavy burdens upon England's coastal towns, and many people who were unable to pay fled the country. In 1637, the sheriff of the county of Suffolk reported Josias Firmin of Polstead, a village three miles northeast of Nayland, as a defaulter, having run away. This Josias is most likely the one who came to Boston to be servant of John Winthrop (who had come from Groton, five miles east of Sudbury), took the oath of a freeman on May 13, 1639, and was admitted to the church on June 6, 1640. If our Giles was of the Nayland branch of the family, this Josias may have been his nephew. See "N. E. Hist. and Gen. Reg.," Vol. 3 (1849), page 187, and Vol. 56 (1902), pages 182–183.

were yielding to wild experiment that bred both hope and despair in fools and demanded much tactful patience in the wise; and the yeast of unrest was fermenting the rush of poets who still startle the world with their genius. Geographically horizons were likewise broadening: gangsters and pirates like Drake and Hawkins were charting the seas and making them unsafe for foreign traders, especially the Spaniards; and certain British minds, for divers reasons, some motivated by an itching for wealth and power, others by nervousness and impatience, were already thinking about the extension of Britain's domains in the New World.

But ordinary daily life, as usual, went on about its business. In the midst of such excitement, young Giles elected to become an apothecary, even though the trade offered prospects that could not have seemed very bright. Perhaps his father had been in the profession before him; perhaps some practicing friend of the family was willing to take him on as apprentice. Whatever his reason, it is interesting to consider what were his prospects.

During the reign of Henry VIII (who, like his daughter Elizabeth, was fond of inventing compounds and plasters in the royal laboratory), a physician named Bulleyn had written: "The apothecary must first serve God, foresee the end, be cleanly, and pity the poor. His place of dwelling must be cleanly, to please the senses withal. His garden must be at hand with plenty of herbs, seeds, and roots. He must read Dioscorides. He must have his mortars, stills, pots, filters, glasses, boxes clean and sweet. He must have two places in his shop: one most clean for physic, and the base place for chirurgic stuff. He is neither to decrease nor diminish the physician's prescriptions. He is neither to buy nor sell rotten drugs. He must be able to open well a vein, for to help pleurisy. He is to meddle only in his own vocation, and to remember that his office is only to be the physician's cook."[1]

We hear no protests by the apothecaries at this definition of their status. They were not organized into a separate, self-conscious body. Sixteenth-century legislation gave to members of the Faculty of Medicine the right to practice medicine, pharmacy and surgery; and the term "apothecary" was not applied to the member of a distinct profession, but to the assistant or apprentice who compounded his master's prescriptions, prepared stock remedies, and performed minor surgery.

This work somehow appealed to young Giles. Just about the time that he was learning to serve God and be neat and clean, planting herbs in his garden, studying Dioscorides, collecting mortars, stills, pots, filters, glasses, bottles, and boxes in his workshop, opening veins, earning enough soon to support a wife and family, his fellows in the trade, after having worked as "cooks" for a century or more, felt ready to assert some independence. In 1606 they formed a common guild with their hereditary rivals in the business of importing drugs and spices, the grocers; but they still had to show the ingredients of their compounds to any physician who insisted upon an inspection. Though they found little satisfaction in associating with the domineering grocers, they had cause for hope, since James I (who had come down from Scotland to be king in 1603) had as personal physician a foreigner of Paracelsian leanings who respected and pitied them. This doctor won for them the king's interest, and in 1617 James granted to the apothecaries a

[1] Quoted in Charles H. LaWall, "Four Thousand Years of Pharmacy" (Philadelphia, J. B. Lippincott Company, 1927), page 208.

charter for an independent and exclusive guild. Later, irked by the continued fuss raised by the jealous grocers, the King told them bluntly that no matter what medieval precedent they had for putting their noses into the drug business, they could do so no longer, for they were merely merchants, whereas the business of the apothecary was a mystery (which is to say, an art).[1]

This marked improvement in his profession must have been agreeable to Giles Firmin. But in the meantime one thing in old Bulleyn's instructions to apothecaries he refused to obey: he meddled in more than his chosen vocation. He meddled with local politics, taking active part in managing the town of Sudbury, as councilor or alderman,[2] presumedly through the favor of his distinguished uncle Richard. And—possibly moved by Bulleyn's advice to "foresee the end"—he meddled with religion, for he was a sincere and pious man, far more concerned with souls than with sales.

His home was within the metropolitan radius, strongly influenced by London opinion, that had been first willing to protest with Henry VIII against the ancient religious heritage of England; but the same district had been among the first to protest against what the new arbitrary state religion offered instead. Whether Giles turned Puritan (with all the enthusiasm of a new convert) or became strengthened in Puritanical views bequeathed him by his parents makes little difference: he was first a religious man and afterward a pharmacist; and though his profession held brighter and brighter prospects, in the face of corruption all round him he became more and more worried about the problem of how to lead a godly life.

His son, destined to go the father one better in the practice both of medicine and godly living, had been born in 1614 or 1615. (Who the mother was we do not know, nor when she died, though we may be sure that she did not live to accompany her husband to Boston.) As the boy grew old enough to heed, he must have heard his father discuss the settlement of New Plymouth by refugee members of the Puritan faith. And in addition to religious instuction, the boy undoubtedly received medical training from his father. In 1626 or 1627, being above twelve years old, he left home to attend school; and three years later, on December 15, 1629, he entered Emmanuel College, Cambridge University.[3]

From a sequence of known facts we may infer the conduct of father and son during the next four years.

When a Royal Charter for the establishment of a colony in New England made the Puritans believe that vague dreams of developing their dreary Utopia (dreams already encouraged by the quiet success of New Plymouth) had a fair chance of being realized, John Firmin, the presumed cousin of our man, decided to sail with the first wave of settlers in 1630. Two years later, prompted by we know not what curiosity, dissatisfaction, or ambition, the boy Giles, Junior, now about eighteen years old, decided to follow him, and on April 8, 1632, he embarked

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[1] See LaWall, Chapters 6 and 7.

[2] The remark by Giles, Junior, quoted below, that his father had once been "a Gown-man in a corporation" may have had in mind the office of selectman in Boston, but the phrase is in the language of old England rather than new: according to the Oxford Dictionary a "corporation" could mean the "mayor, alderman, and councillors of a borough or incorporated town" and in one obsolete use "gownsman" denoted "a member of a municipal corporation."

[3] "N. E. Hist. and Gen. Reg.," Vol. 25 (1871), pages 52–53.

for Boston on the *Whale*, in company with the most influential Puritan minister in his native county, the Reverend John Wilson, arriving here on May 26th.[1] He joined the church promptly,[2] but did not take the oath of a freeman, not being yet of legal age.

We may guess that the boy was startled to discover settlers everywhere suffering from diseases brought from England and bewildering new organic ailments fostered by a change of diet, climate, and habits. There were few skilful physicians; anyone with even but a smattering of the art was welcome to share the continuous burden of trained practitioners like Governor Winthrop of Boston and Samuel Fuller of Plymouth, using remedies long standard in Europe, when available, or substitutes newly learned from the Indians, to combat what they recognized as fevers, colds, indigestion, rheumatism, scurvy, small-pox, and other persistent evils.

Young Giles quickly saw how he might be of most use to the colony. He may have written his father, urging him to come over and share in the good work. Whether he did or not, it was not long before Giles, Senior, closed his business in Sudbury, gathered his books, instruments, and store of drugs, and embarked for Boston. He was admitted to the Boston church some time between October 11, 1632, and September 8, 1633,[3] and probably he and his son lived for a time and worked together here.

The wilderness of Massachusetts, of course, had offered no excuse at first for formal places of business. Farmers, builders, preachers, indeed, went right to work, and anyone who knew anything about medicine or nursing was kept busy. But it is not surprising that we hear nothing of Firmin's opening a shop in Boston.[4] The town was rapidly taking shape, with good streets and fine dwellings, but Firmin could as likely have wielded axe and hoe as spatula and pestle. Still, we may be practically certain that his professional knowledge was respected and put to use by the desperate citizens, and we have every right to assume that Giles Firmin emerged from the obscurity of a pharmacist in Sudbury to the prominence of one of Boston's few trained physicians. A physician as well as an apothecary is what his son later became here.

Very likely it was the father who urged his son to pursue medical studies in England. Before October 10, 1633, the boy had gone, and the father carried on his work alone. He was not to see his son again. Late that winter, on March 4, 1634, he swore the oath of a freeman,[5] and soon thereafter his value to the community was recognized by his being made a selectman, for a list of the ten selectmen present at a meeting held on July 1st includes his name.[6] Then suddenly he knew his time was up. Perhaps like Doctor Fuller of Plymouth he took some fatal malady from a patient. To the grief of his friends but satisfied of his reward, he fell upon his bed and called to God for relief. On October 6, 1634, at a town meeting, Richard

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[1] "N. E. Hist. and Gen. Reg.," page 53.

[2] Ms. records of the First Church in Boston.

[3] Same.

[4] The first drug store in Boston is generally supposed to have been that of William Davis, on Washington Street near State Street in 1646.

[5] "N. E. Hist. and Gen. Reg.," Vol. 3 (1849), page 92.

[6] Same, Vol. 4 (1850), page 124.

Bellingham, Esq., was chosen a selectman "in place of Giles Firmin, deceased."[1]

The only other reference to him so far discovered lies near the end of a book written years afterward by Giles, Junior, in which he cites his father's character as proof that a man may be devoutly religious even though he may neglect some particular observance. The unspecified "duty" referred to in this passage perhaps means "religious meditation"—a subject much in the writer's thoughts:

"I called to mind that my own Father, during the time I lived with him (unless it were on the Lord's day) did not perform the duty; what he did after I cannot well tell; but yet he was a man who kept his secret communion with God, had a heart for God, and a tongue for God (as sometimes being a Gown-man in a corporation, he had occasion to appear for God); while he lived in the world, was above the world; when he came to leave the world, he would several times send up short prayers to his Father: When wilt thou send thy Servant to fetch me home? With a smiling countenance he entertained Death, having some fore-tastes of what he was going to possess, by that expression of his: I shall have as much glory as ever I can bear. When he was dead, his Minister, who wrote to us the news of his death, said this of him: *He lived much desired, he died much mourned for.* Yet this my godly Father would scarcely be esteemed for a serious Christian by some, for not performing that duty according to the question; though I suppose a year or two before his death he did take it up, but then I was far distant from him."[2]

Thus passed the first apothecary known to have set foot upon New England's soil: a man who left no lasting impression upon the world but who carried in his features a promise of glory in afterlife; who was much loved by all associated with him; and who gave to his more distinguished son an example and training in two careers, the one ministering to the flesh, the other to the soul.

KAPPA PSI-PHI DELTA CHI GRADUATE CHAPTERS MEET.

The Alumni Chapter of Phi Delta Chi Pharmaceutical Fraternity and the Boston Graduate Chapter of Kappa Psi Fraternity held their Second Annual Interfraternal Meeting at the Massachusetts College of Pharmacy in Boston, February 18th.

Dean Howard C. Newton presided as Chairman. R. D. Hetterick presented two interesting films, one on Cod Liver Oil, and the other, "The Standardization of Digitalis." Regent Charles MacCullom of Kappa Psi, Secretary Joseph H. Goodness of the Alumni Association and William Acheson of Phi Delta Chi carried the greetings of their organizations to the group. The guest speaker for the evening was Professor Edwin Wilson Hadley, noted member of the Massachusetts Bar and professor at Northeastern University Law School. His subject was "Law and Its Relationship to Society."

Herbert C. Packard was the recipient of a copy of Scoville's "Art of Compounding." Mr. Packard was the oldest fraternity man present, a brother of Kappa Psi and a member of the Class of 1892.

Among the invited guests were Augustine Lawlor, John Walsh, John R. Sawyer and Herbert Bowdoin.

The evening was concluded with a buffet luncheon.

ROBERT A. WALSH, *Secretary*, Alumni Chapter, Phi Delta Chi.
GEORGE F. ARCHAMBAULT, *Secretary*, Graduate Chapter, Kappa Psi.

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[1] Winthrop, "History," foot-note, page 114.

[2] Giles Firmin, "The Real Christian, or a Treatise of Effectual Calling" (Boston: printed by Rogers & Fowle for J. Edwards in Cornhill and J. Blanchard at the Bible & Crown in Dock Square, 1742), pages 314–315.

A NOVEL PHARMACEUTICAL ORGANIZATION.*

BY OSCAR LODDY.

Washed in the West by the turbulent Baltic Sea, bound in the East by Soviet Russia, the democratic Republic of Estonia is one of the most progressive small nations in Northern Europe. Though close to Red Russia, Marxian dialectics have been manfully resisted in Estonia, as have been socialism, fascism and other isms prevalent in the modern world (1). The economic structure of the country is based on sound capitalistic principles of private property and individualism in enterprise. Estonia is not a populous country. The number of its citizens does not exceed much over a million; yet it has won the favorable attention and respect of other nations for its rapid progress in many lines of human endeavor and advanced social legislature. It is not our business to examine any of those here. Our concern is with a novel pharmaceutical organization originated in Estonia, "The Estonian Chamber of Pharmacy."

Though the country is small, it can boast of six pharmaceutical associations, around which are gathered different elements within the profession (2). There is an association of drug-store proprietors, an association of employee pharmacists, an association of German speaking pharmacists, an association for scientific pharmacy, an association of assistant pharmacists and an academic pharmaceutical association. Instead of being under-organized as in America, pharmacy in Estonia for a number of years was over-organized into many, often contentious, factions. In such a situation no association was qualified to speak for pharmacy as a whole. Paradoxically, in a number of cases the opposition to attempted pharmacy legislature came from rival pharmaceutical organizations. The first attempt to form a united pharmaceutical front was made by a call to associations to unite into a national federation of pharmaceutical associations. This, however, was doomed to failure, since only three organizations joined the federation; the others preferred to stay out. In this somewhat crucial situation, the leading members of the profession, notably Messrs. Wallner, Lill and Dr. Rallesoo, as early as 1931, conceived the necessity of creating a national pharmaceutical super-organization that would be above factional politics, and would be a true representative body of all pharmacists in the country. These gentlemen accordingly evolved the idea of "The Chamber of Pharmacy." Finding that the idea of "The Chamber" was generally favored by the profession, they went ahead and worked out definite rules and by-laws governing this organization, submitted them to proper government authorities, and asked for the charter. At first there was a reluctance on the part of the government to the creation of an organization of this type, and no action on it was forthcoming for a number of years. Finally, in the Fall of 1934, the President of the Republic expressed his approval of The Chamber, and the charter was issued accordingly. "The Estonian Chamber of Pharmacy" began its functions January 1, 1935.

By its charter The Chamber of Pharmacy has many earmarks of a public corporation as related to pharmacy, with definite powers, rights, duties and obligations. It is an instrumentality to increase the efficiency of pharmacy administration, to supply the various wants of pharmacists, and to promote the public health and the

* Section on Education and Legislation, A. PH. A., Dallas meeting, 1936.

general welfare of the profession. Within this sphere The Chamber has certain legislative, executive and judicial functions; has right to impose levies on its members and punish them. On the other hand it owes its constituents protection and help, legal and economical. For this, every member of The Chamber owes it undisputed obedience and fealty. "One for all; all for one" is the corner-stone of this organization.

Every registered pharmacist, if he desires to practice, must be a member of The Chamber and pay his dues promptly. This does not apply to pharmacists in government service, to whom, during the tenure of their office, the membership is closed for reasons of public policy.

The Chamber maintains itself by levies from various sources, of which the most important are membership fees, fines imposed by The Disciplinary Court of The Chamber, and a levy on prescriptions (one cent on every prescription filled).

The Chamber functions through its legislative, executive and judicial set-up. The legislative power and the appointment of commissions and committees is in the hands of *The Council of The Chamber*. It consists of 20 members elected for 4 years. Executive functions fall on the shoulders of *The Board of Directors*, composed of the President, Vice-President and Secretary. The tasks of The Board are of administrative nature, such as enacting the decisions and rules of The Council, collecting membership dues and other levies, representing The Chamber in courts of law and government bureaus, maintaining an employment agency for pharmacists, etc. The judicial power is vested in *The Disciplinary Court* of five members. This court has jurisdiction over practicing pharmacists, and acts in breaches of professional ethics and in cases of improper conduct outside of professional duties. The Court has four remedies at its disposal: Warning, reprimand, fine not over 300 kronen (about $80.00), and the suspension of the license for not over a year.

As to avowed purposes of The Chamber of Pharmacy, Mr. K. Jürison, the president of The Board (3), lists the following: (1) to promote the lawful practice of pharmacy in the country; (2) to stand up for the rights of pharmacists and to protect the interests of the whole profession; (3) to represent pharmacy in government bureaus and other administrative agencies; (4) to promote domestic drug manufacture and collecting of crude drugs; (5) to keep a register of pharmacists and their business enterprises; (6) to maintain a welfare department for the benefit of pharmacists, their families and help, who may need assistance whether due to old age, sickness or loss of capacity for work; (7) to elect from among its members pharmacists for public service, as occasions may arise; (8) to issue certificates and other information to members, who require them; (9) to collect and publish statistics relating to pharmacy; (10) to clarify misunderstandings between the members and maintain high professional code of ethics.

R. Wallner (4) summarized the above as follows: "What is the purpose of The Chamber? To serve as an intermediary between the government and the profession of pharmacy. Any proposed legislature relating to pharmacy, be it national or local, is sent to The Chamber for comments and approval. Likewise the board of directors of The Chamber may sponsor new laws which the profession wishes to be passed by The Parliament. The Chamber protects the interests of pharmacists. It supervises that the members of the profession abide by laws and observe the code of

ethics. The Chamber has a disciplinary court, where are discussed offences against law and ethics, and punishments meted out. The punishments of The Chamber, however, have to be approved by The Administration of Public Health and Welfare. With the aid of The Chamber the pharmacists in this country desire to establish an independent pharmacy administration, reduce the excessive taxes imposed on drug stores, and generally raise the ethics of the profession."

Even though The Chamber performs certain functions of administrative nature, it is not an organ of the government, nor does it encroach upon the authority of The Department of Pharmacy in The Public Health Administration. It is a chartered corporate body for mutual protection, benefit and discipline. It complements the government only where the latter leaves off. Neither does The Chamber displace the existing associations, though many of the former assumptions of associations are of necessity curbed. Says President Jürison (3): "By establishing The Chamber of Pharmacy, there was created a definite representative body for the profession of pharmacy in the country, in which all the colleagues are obliged to take part and coöperate. Not only that; every pharmacist is responsible to The Disciplinary Court for his words and deeds...(5). The Chamber must develop in its members love and the sense of responsibility for their work and calling... It must stretch out its helping hand to those colleagues, for whom the struggle for existence makes difficult to preserve the professional integrity..."

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(4) Wallner, R., A personal communication to the author, September 22, 1935.

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"OIL FOR THE WHEELS OF PHARMACY."

An article by R. L. Swain appears in the March issue of the *Medical Economics* which it would be well for both physicians and pharmacists to read. In closing, he admonishes:

"Never criticise the pharmacist in the presence of the patient. First of all, it is usually unfair, unjustified and uncalled for. While it may do the pharmacist harm, it may do the physician equal harm. It so happens that the patient is often as friendly with the pharmacist as with the physician. The physician should be just as considerate of the reputation of the pharmacist as he is of his own." He concludes:

"My final plea is that medicine and pharmacy seek to function as colleagues striving for a common goal. That each diligently cultivate that spirit of accord, that spirit of mutual understanding and obligation, that spirit of purposeful coöperation which their respective abilities and capabilities certainly suggest as sound, sensible and wholly desirable."

GERMAN APOTHECARIES DAY.

Apothecary Day will be celebrated in Germany during the end of June 1937. This celebration will be especially featured in Essen. A large celebration is planned and among the questions that will be studied are those relating to the new Legislation.

PHARMACY DRAMATIZED.

Drugs and the part they play in pharmacy are dramatized in an exhibit at the Clinton branch of the Newark Museum. Medicinal plants, as well as modern pharmaceutical equipment, are described in the exhibit.

THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

ERNEST LITTLE—CHAIRMAN OF EXECUTIVE COMMITTEE, A. A. C. P., EDITOR OF THIS DEPARTMENT.

AT THE annual meeting of the A. A. C. P. held at Dallas, Texas, last August, Professor DeKay of Purdue University presented the following paper before the Conference of Teachers of Pharmacy. Although it is intended primarily for teachers of pharmacy it should prove of interest to all individuals in the field of pharmaceutical education.

Most of us willingly admit that many worthy objectives can be obtained by a variety of different methods and that certain destinations may be reached by various avenues of approach.

Without an adequate knowledge of the various methods now employed and the results obtained by them, one cannot arrive at the wisest decision as to what his policies and procedures should be.

Professor DeKay's suggestions should prove of special interest to teachers who are engaged in pharmacy laboratory instruction and of general interest to all.—ERNEST LITTLE.

A STUDY OF PHARMACY TECHNIQUES.

H. GEORGE DEKAY.*

The curriculums of the schools of pharmacy are so arranged that there are repetitions of laboratory techniques and operations. The teacher of the beginning course is concerned in starting the student right. The courses in pharmacy are so related that the procedures gained in one course can be used in those that follow. The first impressions are usually retained over a long period of time. The students' interest in pharmacy is formed in the first year and it may oftentimes be a reflection of the instructor's interest in the subject. The teacher's concern should be in performing the task to the best of his ability and his reward will be the satisfaction of a job well done. It has been a problem for him to determine how much of the basic training is carried over into future courses.

In this respect, Charter's Report is worthy of consideration. It is accepted in pharmacy as a survey of the field and a great deal of knowledge of the needs of the student should be obtained from it. In the section on Operative Pharmacy it states that "A pharmacist should possess a general knowledge of the methods of manufacture and the physical properties of all preparations sold by him." This survey was made of pharmacy. The data was compiled from a study of 17,000 prescriptions collected from all parts of the United States. It should be an acceptable estimate of the needs of the profession.

From this data one can see where many conclusions could be drawn as to the necessary techniques needed by the pharmacist. It states that "after the list of preparations was prepared the next step was to study them in order to develop what knowledge is needed to make them." Among the things listed are official English titles, synonyms, percentage strengths and the active constituents. This same report states, "The pharmacist needs a very high degree of skill in the techniques of these operations and an accurate familiarity with the closely associated facts listed."

* College of Pharmacy, Purdue University, Lafayette, Indiana.

According to this report, "there is a mass of information and techniques which the student can learn in practice. This information can be learned best and most quickly under guidance. The pharmacist needs a very high degree of skill in the use of the various operations connected with compounding and dispensing of prescriptions and manufacturing those preparations recommended to be made in the operative pharmacy study." There is a question in the minds of many of us just where the student is to get this experience or practice. Many states do not require apprentice or drug store experience. The experience, for those who do not get it in drug stores, is gained in the schools of pharmacy under guidance of the instructors and teachers. Many of the students obtain their first touch of prescription work in the course in dispensing.

REPETITIONS IN TECHNIQUES.

A study of the content of courses will reveal a similarity in the type processes and techniques which are used in completing the work in the laboratory. The repetition in these courses is of great value to the student if he can be shown wherein they are related. We know the value of repeating and it has oftentimes seemed that we repeated certain directions until they had become rote but we must realize that students are pliable subjects who are being taught by many instructors. The instructors have ideas of performance and application which are, in part or as a whole, different from those of his colleagues. The question of whether a student should have a number of different instructors is debatable. We know that a wider variety of experiences tends to educate an individual and because of this it is, perhaps, advisable for the wide range in courses.

The methods of the pharmacy teacher may not be those used by the chemistry or biology instructor, and the student may become confused as to which method is the correct one to use. The laboratory techniques and methods of approach are similar in the pharmacy courses because the student is usually under the direction of one professor or instructor. There should be a correlation in the pharmacy laboratory which could be measured.

This correlation should be measured objectively. There have been no tests or measuring sticks made for such a means of testing. According to Tyler, in his Constructing Achievement Tests, "adequate and reliable methods for testing the amount of information which a student remembers have been developed recently in many fields of subject-matter. Few tests are yet available for measuring the degree of laboratory skill attained by the students. The important problem in higher education is the permanence of learning. Early investigations of the learning of nonsense syllables showed a rapid rate of forgetting as soon as the learning exercises were discontinued. Studies of the retention of information acquired in college courses have been made in several universities, but no attempt has been made to compare the degree of forgetting which takes place with reference to the remembering of different types of material acquired by college students."

THE PHARMACY COURSES.

The first course in pharmacy at Purdue University embraces a foundation in pharmaceutical arithmetic, Latin and the fundamentals of pharmacy. The student becomes conversant with the United States Pharmacopœia and the Na-

tional Formulary. He is taught the use and manipulation of the working tools of his profession. In the first semester, he obtains instruction and training in the common techniques which include weighing and weight systems, measures and measurements, the properties of liquids and solids, methods of subdivision, characteristic properties of solutions, methods of extraction and separation including percolation, distillation, calcination, incineration and sublimation, and many other type processes of manufacture.

In the second semester he is given assignments which cover the manufacture of a number of official preparations which he will use in pharmacy. The technique of manufacture is the same for the beginner as it is for the more advanced student. He is beginning and is therefore not entirely conscious of what value the work will have on his future training. The student is made pharmacy-conscious in the work because if his interest is developed at this time, there will be a greater amount of retention. He is interested in making preparations which are used in his profession and at this time the stressing of what the prescription must be and the care needed in its compounding should make a deep impression which may be permanently retained by the student.

The advanced courses are given in the junior and senior years. The student is assigned to one semester of prescription practice and one semester of manufacturing pharmacy. The question of the carrying-over of habits, skills and techniques from previous courses becomes an important one. In the course in prescription practice he is required to fill a large number of prescriptions which are not made for his special benefit. They are compiled from a large number of prescriptions written by physicians in the State of Indiana and elsewhere. The student is impressed with the variations and types of prescriptions which he is to fill.

The ability of the student to retain part of the technique of manufacture is soon apparent. It is usually necessary for the instructor to give aid to each student until he has again reclaimed the skill which he had obtained as a freshman student. The first part of every semester is given over to a review and application of the laboratory work of his previous semester. Those students who have become pharmacy-minded do not find it very difficult to regain their ability to fill prescriptions. Some of the students have carried over many of the bad habits and their work is oftentimes sloppy and lacks that degree of neatness and finish which the pharmacist needs in his work.

In all courses of pharmacy the methods of manufacture are the same as those of the beginning course with the exception that the quantities of finished products are much greater. The student must apply the knowledge learned in the first year to the problems which arise in the advanced work. The skill gained in pharmaceutical arithmetic must be used to enlarge formulas. His knowledge of weights and measures is needed in the measuring and weighing of his larger quantities. He needs his training of making changes from one system to another. The general laboratory techniques of filtering, percolating, mixing, etc., are needed at this time.

THE VALUE OF EXPERIENCE.

We have found that the student who has had some drug store experience between his freshman and junior years will usually do a better job in the manufacturing of preparations than one who has had no experience. The one who has

worked in a drug store has obtained certain values of the professional attitude which aids him in his work. He has gained a realization of the responsibility of his position or become pharmacy-conscious. It is our observation that the student who has had this additional experience with the public will attack his problem with a degree of certainty, while the student who has not become pharmacy-conscious will possess a degree of fear and uncertainty. The finished products may be of an equal quality, yet the amount of time consumed in their manufacture will be considerably different.

APPLICATIONS OF TECHNIQUE.

An example of how the student may apply his previous training and experiences to new situations is clearly shown in the manufacture of tablets by machinery. He has had no experience in this definite assignment yet he has had all of the experiences needed for its completion. The problem is analyzed by the student in the light of these situations. The weighing of the quantities and mixing of the ingredients are the same as those used by him in his first year. The granulation of the powder can be compared to the granulation of effervescent salts. The new problem is the compressing of the tablet. He is now able to apply his experiences of the manufacture of tablet triturates to this new problem. The questions of pressure, disintegration, appearances of finished product, *etc.*, are the same as those of the former problem.

Another example of laboratory technique is found in the manufacture of emulsions. He is taught the procedures and the need of care in manufacture, yet he does not fully realize just why these things are necessary until he has homogenized an emulsion. He is able to see the finished product under the microscope and can compare the hand-made emulsion with the one made by machinery. He sees the difference in the size of oil particles and the differences in texture of the finished product. The keeping qualities of the two emulsions are stressed at this time.

The methods of filtration, measurements, *etc.*, are used by the student in the pharmaceutical chemistry courses. The analytical courses require the use of the analytical balance and apparatus commonly used by the pharmacist. His methods of solution, precipitation and decantation are used in the qualitative analysis laboratory. The course is based upon precipitation, solubilities and separation of component parts. He is taught the methods of chemical reactions and how to recognize the changes which occur. The characteristic properties of inorganic solids used in pharmacy are explained to him. He is given techniques needed in his future work in pharmacy.

He uses his qualitative analysis training in the study of incompatibilities found in prescriptions. From his training he should be able to recognize any change which might occur in compounding. The problem of ointment manufacture is again brought to his attention and he now understands why he was directed to use a bone spatula in place of one made of iron. The chemical changes which occur in the manufacture of ointments containing iodine, mercury, benzoic or salicylic acid when an iron spatula has been used will show in the finished product. The responsibility, training, skill and technique needed in the practice of pharmacy becomes something real at this time.

In the prescription practice laboratory a large number of incompatible pre-

scriptions are studied and the student is able to apply the qualitative work to this course with a degree of understanding. He is more able to realize the care needed in filling prescriptions containing alkaloids and their salts. Numerous other problems of a similar nature could be cited.

There are many situations and experiences gained in the beginning courses which can be related to those used in the advanced work in pharmacy. A more complete correlation of techniques could be worked out if a series of tests or measurements were made and then applied to both the beginning student and those of advanced training.

CALCIUM DETERMINATION IN BLOOD SERUM.*

BY C. W. EDMUNDS, M.D.

(SUGGESTED FOR U. S. P. ADOPTION.)

Place 2 cc. of clear blood serum, 2 cc. of distilled water and 1 cc. of a 4 per cent ammonium oxalate solution in a graduated, 15-cc. centrifuge tube with an outside diameter of from 6 to 7 mm. at the 0.1-cc. mark and mix. Mixing is facilitated by giving the tube a quick, jerky, whirling motion. Allow it to stand for thirty minutes. Again mix the contents and centrifuge for about five minutes at 1500 revolutions per minute. Carefully pour off the supernatant liquid and, while the tube is still inverted, allow it to drain in a rack for five minutes, resting the mouth of the tube on a pad of filter paper. Wipe the mouth of the tube dry with a soft cloth. Stir up the precipitate and wash the sides of the tube with 3 cc. of dilute ammonia (2 cc. of stronger ammonia T.S. to 98 cc. of distilled water) directed in a very fine stream from a wash bottle. Centrifuge the suspension and drain again as before. Add 2 cc. of approximately normal sulfuric acid by blowing it from a pipette directly upon the precipitate so as to break up the mat and facilitate solution. Place the tube and contents in a bath of boiling water for about one minute and titrate with one hundredth-normal potassium permanganate to a definite pink color which persists for at least one minute. During the course of the titration the contents of the tube must be maintained at a temperature of from 70° to 75° C. A micro-burette, graduated in 0.02 cc., should be used.

Hundredth-Normal Potassium Permanganate.—It is essential that the potassium permanganate solution be carefully prepared and standardized as directed below:

Dissolve approximately 4 Gm. of reagent potassium permanganate in 1000 cc. of redistilled water in a thoroughly clean Florence flask. Insert a funnel, covered with a watch glass as a condenser and digest for several hours at approximately the boiling point. Cool, allow it to stand over night and filter with gentle suction through a 3-inch Buchner funnel lined with ignited asbestos. Transfer this to a perfectly clean glass-stoppered bottle and keep it in a dark place. This serves as the stock solution. From this stock solution approximately hundredth-normal potassium permanganate is prepared by dilution and standardized against hundredth-normal sodium oxalate which should keep for several months.

Hundredth-Normal Sodium Oxalate.—Dry reagent sodium oxalate in an oven at from 100° to 105° C. for twelve hours. Dissolve exactly 0.67 Gm. of this oxlate in redistilled water, add 5 cc. of reagent sulfuric acid and dilute to 1000 cc. Mix well. Transfer exactly 25 cc. of this solution to a 100-cc. Erlenmeyer flask, add 1 cc. of reagent sulfuric acid, warm to about 70° C. and titrate with the permanganate solution.

The permanganate solution should be frequently restandardized. A fresh solution of hundredth-normal potassium permanganate should be prepared from the stock solution by dilution, each time the reagent is to be used.

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* See page 202.

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council." —Part of Chapter VI, Article VI of the By-Laws.

ARTICLE III of Chapter VII reads: "The objects and aims of local branches of this Association shall be the same as set forth in ARTICLE I of the Constitution of this body, *and the acts of local branches shall in no way commit or bind this Association, and can only serve as recommendations to it.* And no local branch shall enact any article of Constitution or By-Law to conflict with the Constitution or By-Laws of this Association."

ARTICLE IV of Chapter VII reads: "Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."

Reports of the meeting of the Local Branches shall be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten with wide spaces between the lines. Care should be taken to give proper names correctly and manuscript should be signed by the reporter. *Please advise us of changes in Roster and mail reports promptly.*

BALTIMORE.

The February meeting of the Baltimore Branch, A. PH. A., was held on the 16th, at the School of Pharmacy of the University of Maryland: President A. N. Hewing presiding.

Decidedly adverse weather conditions prevailing on this date operated to reduce attendance of members to a fraction of the number usually present at these meetings. The previously scheduled address for the evening was canceled, and a substitute program provided. However, those hardy members who braved the first really heavy snow storm which had visited this locality during the winter to attend were well repaid for the inconvenience and effort involved.

An interesting address and discussion on "Aromatic Vehicles and Their Uses in Prescription Compounding" was given by Prof. Marvin J. Andrews, of the School of Pharmacy.

Various new and old vehicles, with compounded mixtures and solutions containing these, were effectively displayed. The materials displayed were used by Professor Andrews to illustrate points made in his address; which might well have been termed a post-graduate lecture on the proper use of aromatic vehicles in the preparation of medicines. One interesting item included in this address for the benefit of retail pharmacists was the demonstration of a simplified method suggested for use in calculating the quantities of high and low alcoholic content Iso-elixir required in filling prescriptions calling for mixtures containing tinctures and fluidextracts of varying alcoholic strengths.

During the discussion which followed his address the speaker exhibited a copy of bound reprints of the series of articles by outstanding physicians on the treatment of various ailments with U. S. P. and N. F. products which have been quoted as references in several late releases of suggested prescription forms sent out to physicians by the Maryland U. S. P. and N. F. Publicity Committee. The articles referred to have been published in the *Journal of the A. M. A.*, under the joint sponsorship of officers of the American Medical Association and the Revision Committee of the U. S. P. In addition to constituting a desirable and welcome contribution to current medical literature, such articles by prominent physicians are providing an ethical background for the activities of numerous state and local committees organized to popularize the use of official drugs and preparations by practicing physicians.

Professor Andrews stated that while it was not the province of pharmaceutical organizations to offer information regarding the therapeutic uses of drugs to physicians, a real service might be rendered in providing suitable vehicles for their administration, and in suggesting methods of compounding which will insure both palatable and therapeutically effective medication.

Apparently, not a great number of pharmacists has as yet come to realize the full significance and value of the successful efforts of the Pharmacopœial Revision Committee in obtaining the approval and aid of such prominent medical authorities in the publicity campaign inaugurated by the committee last year. This campaign is designed to familiarize physicians

with official drugs and preparations, and to publicize to the medical practitioner the therapeutic advantages inherent in these standardized products. The whole-hearted support of the Editor and publication committee of the *Journal of the American Medical Association* in publishing and featuring these authoritative articles on the therapeutic uses of official drug products certainly deserves the commendation and moral support of all pharmacists. Professor Andrews stated that the Maryland U. S. P. and N. F. Publicity Committee, of which he is Chairman, has been making extensive use of the material published in the *A. M. A. Journal*. It would of course be impossible to evaluate results to date of this new form of publicity, but he regards these contributions and efforts as of prime importance to both medicine and pharmacy.

ROBERT S. FUQUA, *Secretary*.

CHICAGO.

The monthly meeting of the Chicago Branch was held February 16th, at the University of Illinois College of Medicine.

About eighty-five members and friends were present to hear the lecture delivered by Dr. Ralston, connected with the Department of Experimental Medicine, Parke, Davis & Company.

Dr. Ralston chose as his subject "Fifty Years of Scientific Pharmacy."

The story of the advances made in scientific pharmacy was told by Dr. Ralston by beginning with the corner drug store of 1850–1866.

At about this time a few retail druggists began to think of the opportunities present in supplying druggists with pharmaceutical preparations and of marketing new medicaments. These men started the forerunners of the present-day large pharmaceutical manufacturing houses. The competition of the early day manufacturing houses caused a world-wide search for new drugs to put on the market. From this point the discussion was divided into five successive phases of scientific advancement in Pharmacy.

FIRST PHASE: BOTANICAL STANDARDIZATION ERA.

In the year 1879 the first chemically standardized drug, Ergot, was introduced. By 1833 this list had grown to twenty drugs. In the year 1897 Ergot was standardized by physiological methods.

SECOND PHASE: BIOLOGICAL STANDARDIZATION.

In the years 1880–1900 wholesale discoveries were made of disease-producing organisms and serums and antitoxins were prepared for injection to combat these diseases. Many advances were quickly made in the purification of these preparations after cases of tetanus had been reported, after treatment with the diphtheria antitoxin. Other untoward reactions were reported. Experimental therapeutics were used extensively for the first time during this era to evaluate the strength of medicines and biologicals on animals. This was followed with clinical testing on human beings. A review was given of present-day biologicals to show the advances that have been made since the beginning of this era.

THIRD PHASE: ENDOCRINE THERAPY.

While the thyroid gland was known to the ancients it was not until as late as 1891 that disturbances of this gland were associated with myxedema. In 1855 the adrenal gland was discovered and Addison's disease was described. In the period of 1890–1900 the blood pressure principle of the adrenal gland was discovered. About ten years ago the activity of the cortex of the gland was investigated which led to the introduction of the substance known in medicine as "Cortin." In 1909 the effect of the pituitary gland on uterine muscle was noticed. During the period of 1915–1920 two active principles of the pituitary gland were standardized—the oxytocic principle and blood-pressure raising principle. At the present time twelve to thirteen hormones have been identified in the pituitary gland. Corpus luteum, the male and female sex hormones, pregnant urine extract and the hormone of the parathyroid gland have been identified and prepared as medicaments for hormone insufficiency. Insulin might be classed in this group, discovered in 1922 and only recently marketed as a protamine zinc insulinate that is said to be superior to insulin.

FOURTH PHASE: ACCESSORY NUTRITIONAL FACTORS.

In the year 1897 the disease known as beri beri was associated with the eating of polished rice. In 1912 the vitamin was discovered and named. In the period of 1912–1937 most of the vitamins have been identified and their sources found. Activity is centered to-day in the synthesizing of the vitamins. Cevatimic acid (vitamin C) is now made synthetically. The minerals calcium, phosphorous and iron are known to play an important part in normal body function and are being more thoroughly investigated at the present time. The value of the liver has been discovered and in 1929 desiccated stomach was found to have the same active principle.

FIFTH PHASE: BIOCHEMICAL.

It is the aim of the biochemists to-day to discover the chemical identity of the antigenic factors of the biologicals. Some of the glandular elaborations have been identified chemically. Adrenalin, thyroxin, the male and female sex hormones may be cited as examples.

Attention is called to the close similarity in chemical structure of ergosterol and the female sex hormone.

Dr. Ralston concluded by stating that pharmacy is indispensable to the health of society and that we as pharmacists, must keep abreast of the progress that is being made.

LAWRENCE TEMPLETON, *Secretary.*

NEW YORK.

The February meeting of the New York Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION met February 8, 1937, in the Columbia University College of Pharmacy.

About seventy members and guests were present.

The minutes of the January meeting were read and approved. The treasurer's balance showed $417.94 on hand.

Mr. Hauck reported the applications of Samuel Ushkow and W. Lee Kirschner for membership in the parent association.

Chairman Lehman, of the Committee of Education and Legislation, reported as follows:

"The decision of the New York State Court of Appeals on the Feld-Crawford Law, is being anxiously awaited, and may be reported any day.

"In Congress there has been introduced, the so-called Miller-Tydings Bill, or National Fair Trade Enabling Act, which establishes a Federal Fair Trade Law in such states as have already adopted a state Fair Trade Law. Such a measure takes away the necessity of registration of foreign firms in such states in which a law of that character is in force at present. Hearings were held on this bill before the Judiciary Committee of the House on Friday, January 29th. Speakers of all branches of retail trade were heard in favor of the measure. Those opposed included R. H. Macy & Co., National Dry Goods Association, Namm Department Stores and the National Grange.

"You are urged to write to the New York State members of the Judiciary Committee and the Rules Committee of the House of Representatives. We have no members in the Senate Judiciary Committee from New York.

"The Bill numbers are S. 100 and H. R. 1611. The New York representatives on the Judiciary Committee are Emanuel Celler, Clarence E. Hancock and William T. Byrne. On the Rules Committee is John O'Connor, Chairman, well known for his sympathy in fair-trade matters. You are urged to write or telegraph in favor of the enactment of the law and ask for a favorable report on the part of the Committees.

"The N. A. R. D. is submitting a Model State Robinson-Patman Bill, or Anti Price Discrimination Act as well as a Model Fair Trade Law, for enactment in such states where there has been no legislation as yet.

"The N. A. R. D. is supporting the Colmer Bill H. R. 4214 which will place a Federal Excise Tax on Interstate Sales at Retail; it is aimed against Mail-order Houses. It is understood that Senator Harrison of Mississippi is introducing a companion bill in the Senate.

"The Mississippi State Board of Pharmacy has issued (Nov. 20th) a *Bulletin* favoring the pharmacist manufacturing his own Galenicals. The document shows the difference in cost of their own product against that which is purchased, and in many cases the saving is considerable."

Dr. H. V. Arny moved that a committee be appointed to draw up suitable resolutions on the death of Dr. George C. Diekman, one of the founders of the Branch, and long active in its affairs. The motion was seconded and carried and Dr. Arny was named as Chairman of the Committee.

Dr. Schaefer announced that arrangements for the annual convention of the A. PH. A., to be held in New York this summer, were progressing smoothly.

The joint meeting of the Boards of Pharmacy and the Faculties of Pharmacy of District No. 2 will be held in New York on March 8th and 9th. This offers a conflict with the regular Branch meeting, so the latter has been postponed one week and will be held on Monday evening, March 15, 1937.

There being no further business, President Schaefer introduced Dr. J. Leon Lascoff who addressed the members on "The Recipe Book II and Its Value to the Pharmacist."

At the conclusion of the talk there was considerable discussion. Questions were asked by Messrs. Ligorio, Wimmer, Mason, Seley, Fischelis and others.

A rising vote of thanks was accorded the speaker and the meeting adjourned.

HORACE T. F. GIVENS, *Secretary*.

THE RECIPE BOOK NO. II AND ITS VALUE TO THE PHARMACIST.

The AMERICAN PHARMACEUTICAL ASSOCIATION has ever been alive to the desirability of collecting and making accessible to retail pharmacists the formulas of preparations not included in any other official publication.

As early as 1856 a committee was appointed by the president to collect unofficial formulas and report them to the ASSOCIATION. The efforts of that committee and other committees continuing its work led eventually to the issuance of the present-day National Formulary. The enactment of the Food and Drugs Act made the National Formulary as well as the United States Pharmacopœia official standard publications, and this fact made the publication of a book containing the formulas for remedies not included in the two official books a pressing necessity. Prof. Henry P. Hynson, of Baltimore, had the foresight to urge upon the AMERICAN PHARMACEUTICAL ASSOCIATION the publication of such a book. In 1909, he suggested the publication of "a general druggist recipe book." Professor Hynson's suggestion, together with letters from Leo Eliel and Otto Raubenheimer, on the same subject, were referred to the Committee on Standards for Non-Official Drugs and Chemical Products for consideration and report at the Los Angeles meeting of the ASSOCIATION. In addition the Council recommended that the Committee named devote its early attention to the compilation of a list of useful recipes for druggists' use.

At the Richmond meeting in 1910, it was suggested that the matter of publishing a Recipe Book be placed in the hands of a "Committee on A. PH. A. Recipe Book." This suggestion was brought officially before the Council in the form of a motion made by Franklin M. Apple. According to that motion, seconded by Leonard M. Seltzer, a committee was to be appointed for the purpose of investigating the advisability of publishing a druggist's recipe book by the ASSOCIATION: to define its scope and character, and submit plans and details for the consideration of the Council and the ASSOCIATION. At the end of the first year the Committee had collected about 120 formulas.

In 1915 the original committee of five was enlarged to fifteen members. From 1910 to 1916 approximately 625 formulas had been collected by the committee.

In May 1920, in Washington, a new committee was appointed, with J. Leon Lascoff as its chairman. The new committee on the Recipe Book was enlarged to 25 members. This group was sub-divided into several working committees, each with its respective chairman. In this way each man came in direct contact with the work which interested him.

In September 1923, at the Buffalo meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION, the Chairman turned over a collection of formulas to the ASSOCIATION, and also an exhibit of a large number of preparations with which the members of the committee and the Chairman had experimented. This collection of formulas, as yet, unedited, represented a total of more than fifteen hundred. At the same meeting, Professor Ivor Griffith was elected editor and was requested to assemble and arrange the formulas for publication.

A careful study of these recipes showed the need for reconsideration of their suitability for inclusion in the book, whereupon a Committee on Scope was appointed. This committee deleted some formulas which had outlived their usefulness and supplied others which were more modern to fill the gaps.

During this interval also many other up-to-date formulas were introduced and the completed manuscript was turned over by the Editor to the Council of Association at the Philadelphia convention, September 1926. It was favorably received by the Council and the Committee on Publication was authorized to secure bids on its publication.

The first edition of the Pharmaceutical Recipe Book was brought to conclusion with 777 Pharmaceutical Formulas, 373 Hospital Formulas, 34 Dental Formulas, 66 Diagnostic Reagents and Clinical Tests, 28 Veterinary Formulas, 45 Photographic Formulas, 184 Cosmetic Formulas, 45 Flavoring Formulas, 69 Technical Formulas—a total of 1621 formulas.

At a meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION in Miami, Florida, Chairman J. Leon Lascoff, presented a comprehensive report of the sales of the Recipe Book and also quite a number of new formulas for the succeeding edition of the Recipe Book. A system of revision was prepared at the Miami meeting, and the ASSOCIATION By-Laws were amended by an addition to Chapter VIII which *placed the Recipe Book on the same basis as the National Formulary*. The matter of another edition of the Recipe Book was discussed and it was deemed advisable to prepare a revised edition.

The work of revision, preparatory to the issuance of Recipe Book II, was begun in 1932.

Early in 1933, *Bulletins* containing formulas for the new Recipe Book were sent out for criticism and review. An extensive display of preparations prepared according to the Recipe Book was exhibited at the Madison meeting.

The favorable reception of the Recipe Book was evidenced when in May of 1934 Chairman Lascoff reported that practically all of the copies of the Recipe Book I had been sold and that it was necessary to proceed with the issuing of the second printing. The Council letter of July 19th, announced that the contract for printing and binding the Recipe Book II had been awarded to the Mack Printing Co., Easton, Pa.

The Recipe Book represents the outcome of an effort of the AMERICAN PHARMACEUTICAL ASSOCIATION to place in the hands of the practicing pharmacist a reliable and comprehensive book of recipes applicable to his business. "It is hoped this book will eventually assume the same serviceable and dignified position that the National Formulary has attained in its particular field." The foregoing introductory from the preface of the First Edition of the Recipe Book expressed a hope which has been given assurance by the favorable reception accorded it.

The preparation of a second edition of the Recipe Book was necessitated by the demand for it after the first edition had been exhausted. A revision was prompted by the appearance of the U. S. Pharmacopœia XI and the National Formulary VI, deletions from which were to be included, and a continued desire on the part of the ASSOCIATION to extend the usefulness of the Recipe Book, and suggestions made by physicians, pharmacists, dentists, chiropodists, veterinarians and others for the revision of and inclusion of additional formulas, tables and other data has resulted in an all extensive revision.

The purpose of the Recipe Book is to supply definite formulas for those preparations which are not included in the official books, but which are in fairly common demand in the retail pharmacy, in the hospital pharmacy and in the manufacture of products relative to which druggists are called upon for advice or supply.

An index of more than fifty pages records the number of formulas in Recipe Book II. The work assigned to the sub-committees was divided in part as follows:

No. 1. Decoctions, Infusions, Elixirs, Emulsions, Glycerites, Juices, Mixtures, Vinegars and Waters.
No. 2. Extracts, Fluidextracts, Oleoresins, Resins and Tinctures.
No. 3. Ointments, Pills, Plasters, Suppositories and Effervescent Salts.
No. 4. Ampuls, Lozenges, Tablets, etc.
No. 5. Toilet Preparations, Smelling Salts, etc.
No. 6. Cosmetics, Creams, Manicure Preparations, Preparations for the Hair, etc.
No. 7. Cleaning Fluids, Disinfectants, Insecticides, Soaps, Utility Preparations, etc.
No. 8. Veterinary Preparations.

No. 9. Household Remedies.
No. 10. Photographic Formulas.
No. 11. Agricultural Formulas.
No. 12. Industrial Formulas.

The admission of all formulas was dependent on a vote of two-thirds of the members of the Committee. All the formulas have been tried out and include only preparations that can be compounded by the pharmacist. The titles of preparations have been studied so that each shall represent, as far as possible, the leading ingredients in the formula and therapeutically suggestive titles shall be eliminated. However, the titles from the Recipe Book I have been included in the index. The Recipe Book has received mention in the Standard Year Book issued by the U. S. Department of Commerce. The Recipe Book does not aim to supply imitations for proprietary or trade-marked articles, and permission has been as far as possible received for reprinting institutional formularies.

The arrangement of formulas, as far as possible, is in alphabetical sequence, the English title being accepted as the primary title, the Latin title as a synonym. Other synonyms are added whenever useful. The metric system is generally used but English units are employed where these have become established through practice.

In all formulas, the ingredients that are official in U. S. P. XI or N. F. VI, are to be of the official strength, quality and purity.

Galenicals listed as ingredients, the formulas for which are not included in the official books, are specified as "R. B." and formulas for them are to be found in this edition of the Recipe Book.

Chairman Lascoff closed his remarks with the following:

"It is my earnest belief and my fond wish that the Recipe Book will find its way to the book shelf of every practical pharmacist in the United States. This I know—that every day I receive so many calls from pharmacists for information which is available in this book, that I would consider no pharmacy as being complete without a copy."

NORTHERN NEW JERSEY.

The Northern New Jersey Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION met at Rutgers College of Pharmacy, February fifteenth. This meeting was a symposium on the four phases of pharmaceutical service.

Miss Marie Jannitti outlined and discussed the duties of the pharmacist toward the diabetic patient: Having available reliable food charts to enable the patient to select variety in the diet and still keep within his limitation; providing the proper reagents and necessary information to assist the patient in performing the urine-sugar tests; providing the necessary hypodermic supplies and instructing the patient in their aseptic use; giving information concerning the emergency treatment for insulin overdosage; and cautioning the patient concerning the dangers that may arise as the result of changing from insulin to the new protamine zinc insulin without first consulting the physician.

Arthur Schneider spoke of the services rendered to and through the nursing profession. The two branches of the nursing profession with the greatest potentialities being the visiting nurse and the industrial nurse. Each of these control, directly or indirectly, a large market for the prescription department and for the sick-room and hospital supplies department.

Discussion of the "baby department" was led by Raphael Nacca. Formulas for antiseptic oils, scalp oils, dusting powders, etc., were given. The proper display of the various prepared baby foods for artificial feeding and the prepared vegetables and vegetable juices was stressed as well as the proper bath and clinical thermometers.

Robert W. Rodman discussed the appropriateness of the amateur photography supplies department. Appropriate because there is no phase of this work that is not related either directly or indirectly to the training of the pharmacist. The developing, fixing, reducing and intensifying chemicals are, with few exceptions, the same chemicals that are found in the prescription case. The pharmacist's training in accuracy makes him the logical person for the amateur to turn for assistance in the chemical processes needed to bring out the desired results. As Mr. Rodman is himself an ardent fan in this hobby, he could well speak of the needs and desires of the amateur photographer.

CYRUS L. COX, *Secretary.*

NORTHWESTERN.

A meeting of the Northwestern Branch, AMERICAN PHARMACEUTICAL ASSOCIATION, was held on Monday, February 15th, in the auditorium of the College of Pharmacy at the University of Minnesota. B. R. Mull, the guest speaker, addressed the gathering upon the subject, "Professional Pharmacy." The talk was followed by a short business meeting presided over by Secretary Netz. The resignation of Mr. R. Almin as Chairman of the Section was presented and accepted. Nominations for Chairman of the Section were called for. Professor E. B. Fischer was nominated. A motion that nominations be closed and that a unanimous vote be cast for Mr. Fischer as Chairman was then made, duly seconded and carried. Professor Fischer was declared elected to the chairmanship by Secretary Netz.

REQUEST FROM SYLLABUS COMMITTEE.

It was decided at the Dallas meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION to revise the Pharmaceutical Syllabus, because of recent changes occurring in pharmaceutical lines. The Committee would appreciate from interested individuals comments on the revision work along any of the following lines: (1) Changes in the required and optional subjects both Professional and Basic and time allotted to same (see Syllabus, pp. 16–17); (2) Changes in title and content of the outlines offered in the Syllabus; (3) Deletion of any outlines; (4) New outlines which should be included; (5) Enlargements of the Section on State Board Examinations.

It is only through discussion and exchanges of ideas from those interested in pharmaceutical education can this work be of the greatest benefit to all concerned and devoid of much criticism. Any suggestions will be much appreciated and will receive due consideration.

HENRY M. BURLAGE, *Acting Chairman.*

CALCULATION OF ISOTONIC SOLUTIONS.

BY H. BÖHME.*

The osmotic pressure of dissolved salts cannot be calculated accurately from the molecular weight, even on the assumption that they are completely ionized, and the following table is given to assist calculation. This shows the concentration of dissolved salt required to produce a definite lowering of the freezing point of the solution.

Dissolved Salt.	Depression of Freezing Point.							
NaCl	0–16	0–34	0–51	0–68	0–85	1–03	1–21	1–38
KCl	0–21	0–43	0–65	0–87	1–09	1–32	1–54	1–77
$NaNO_3$	0–24	0–49	0–75	1–00	1–25	1–51	1–78	2–05
KNO_3	0–28	0–59	0–91	1–24	1–56	1–90	2–34	2–60
$Na_2SO_4, 10H_2O$	0–61	1–38	2–13	2–90	3–72	4–51	5–35	6–30
NaI	0–45	0–90	1–34	1–79	2–23	2–68	3–12	3–58
KI	0–46	0–94	1–45	1–96	2–45	2–94	3–44	3–96
$AgNO_3$	0–48	0–98	1–51	2–05	2–60	3–17	3–74	4–31
$ZnSO_4, 7H_2O$	1–17	2–50	3–85	5–29	6–88	8–48	..	..
$Na_2B_2O_7, 10H_2O$	0–36	0–74	1–27	1–84	2–47	..	..	..
$NaHCO_3$	0–21	0–46	0–71	0–96	1–20	1–45	1–69	1–94
$Na_2HPO_4, 12H_2O$	0–76	1–51	2–34	3–18	4–01	..	..	..

The depression of a solution isotonic with blood is 0–56° C.; of one isotonic with tears 0–80° C. For alkaloidal salts and similar compounds in solutions not stronger than 0–1 M, complete dissociation may be assumed without making any error greater than 5 per cent. The depression due to the dissolved compound is then calculated from the formula $1.86 \times$ g. 1000/ML where g. is the weight of dissolved substance, M its molecular weight, and L the weight of solution. The amount of sodium chloride or other substance to be added to make the solution isotonic is then the amount which in solution will give a lowering of the freezing point equal to the difference between the freezing point desired and that produced by the addition of the first compound.—G. M. From *Quarterly Journal of Pharmacy*, July–Sept., 1936.

* *Arch. Pharm. Berl.*, 274, 255 (1936).

NEW CHEMICALS PROMISE AID IN INSECT CONTROL.

A *Press Bulletin* has been issued by the U. S. Department of Agriculture, of valuable information to pharmacists.

"Out of the thousand or so potential insecticides that have come from the chemists' test-tubes in the last few years, three or four now show definite promise as valuable aids to the farmer in his never-ending war on insect pests of crops, particularly fruit. None of them, however, can yet be recommended for general use. Further work must be done to iron out certain difficulties in the economical manufacture or practical application of each, according to Lee A. Strong, Chief of the Bureau of Entomology and Plant Quarantine, U. S. Department of Agriculture.

"The most promising of the department's newest insecticide discoveries," Mr. Strong says, "is phenothiazine, a compound of carbon, hydrogen, nitrogen and sulfur that is easily prepared by combining diphenylamine—a common aniline derivative—and sulfur... The results of tests, though in the main highly encouraging in the Northwest, show the need for more study. Chief advantages of phenothiazine are that it keeps down the number of stings made on fruit by the worms, and that the residue it leaves is less likely than lead or arsenic to injure human consumers of the treated food products. The main obstacle to the wide-spread use of phenothiazine in northwestern orchards is its effect on the skin of those who handle it.

"In the Midwest and East, field tests with the new sulfur compound against the codling moth have given variable and rather disappointing results," Mr. Strong says. However, enough cases of satisfactory control have been reported to justify a continuation of the work.

"Another possible substitute for lead arsenate suggested by the chemists is nicotine in a form that will stick on fruit and foliage long enough to accomplish its purpose..."

Bentonite—a natural clay of volcanic origin, found in Wyoming, California and other nearby states—can be made to unite with nicotine by mixing it with a salt of nicotine, such as the sulfate, dissolved in water. Sprayed on foliage, this suspension of nicotine-containing clay eventually dries to a fine dust that kills the larvæ of the codling moth feeding there. "Nicotine-bentonite combinations," Mr. Strong says, "would seem to be particularly useful in spraying early apples, which do not call for a very large number of applications of an insecticide and do not stand washing for spray residue removal as well as the firmer winter varieties..."

Results with mixtures of nicotine sulfate in oil emulsions have been highly encouraging in the apple-growing regions of the Pacific Northwest and fairly encouraging in the Middle West and East. In the regular spray schedule, however, these mixtures are open to objection on several points. Sulfur fungicides—necessary to combat fungous diseases in many northeastern orchards—cannot be used with them; too many applications may injure foliage; lead arsenate residues cannot be as readily removed if nicotine and oil have been used in part of the season; and last, but perhaps not least, nicotine treatments are expensive.

"Still under investigation by the department are pyrethrum, and the rotenone-bearing plants that came into general use several years ago after chemists had proposed them and entomologists had confirmed their value. The chemists are now trying—so far without success—to work out a way to synthesize the insecticidal principles of pyrethrum, a plant grown in the Far East and imported into the United States by the millions of pounds for use in the manufacture of insecticides. The recent discovery that the formulas for these principles heretofore accepted are incorrect has given a new turn to the research, which now may produce the results desired. Better ways for recovering all of the rotenone from derris and cube—the foreign-grown plants that contain this insecticidal substance—were devised last year."

INTERNATIONAL HOSPITAL ASSOCIATION.

The fifth International Hospital Congress will be held in Paris from July 5th to 11th. Prof. Roussy (Paris) will give a lecture at the first session on the care of the cancer patient in the hospital. At the second session various aspects of hospitals and nursing in France will be dealt with, while at the third session there will be a discussion on how the hospital can increase its income and reduce its expenditure without detriment to its work. At the fourth session the methodical organization of hospital services will be considered, and the last two sessions will be devoted to short papers and discussions. The secretariat of the congress may be addressed at the offices of the Direction Generale de l'Administration de l'Assistance Publique, 3, Avenue Victoria, Paris IV, or through General Secretary Sydney Lamb, 87, Lord-street, Liverpool, 2.

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1936–1937.

Office of the Secretary, 2215 Constitution Avenue, Washington, D. C.

LETTER NO. 9.

February 26, 1937.

To the Members of the Council:

72. Use of Text of N. F. VI. Motion No. 34 (Council Letter No. 8, page 91) has been carried and Lea and Febiger have been advised.

73. Election of Members. Motion No. 35 (Council Letter No. 8, page 91) has been carried and applicants for membership, numbered 109 to 152, inclusive, are declared elected.

74. Life Members. The following have become Life Members through the payment of dues for thirty-seven consecutive years: Frederick William Sultan, William Carl Wendt, Latta K. Snodgrass, William K. Ilhardt, William M. Federmann; and the following became Life Members through the payment of the required fee: L. A. Brown, Joe W. Quillen, Henry P. Busch, Ray E. Schoetzow and George H. Knowlton.

75. Applicants for Membership. The following applications, properly endorsed and accompanied with the first year's dues, have been received:

No. 153, Francis Marion Putnam, 129 Medford St., Malden, Mass.; No. 154, Mrs. Frank A. Goodrum, 2808 W. 14th St., Little Rock, Ark.; No. 155, Sister Maria Dolorosa Kavanagh, N. Y. Foundling Hospital, N. Y. C.; No. 156, Sister Lydia Spain, Providence Hospital, Washington, D. C.; No. 157, Paul G. Stodghill, 319 16th St., Denver, Colo.; No. 158, Monte L. Powell, 295 So. Downing, Denver, Colo.; No. 159, Donald F. Clifford, 730 Majestic Bldg., Denver, Colo.; No. 160, Karl S. Burkett, 2608 E. Colfax, Denver, Colo.; No. 161, Edward J. Carroll, 333 E. 16th Ave., Denver, Colo.; No. 162, William J. Bishop, 820 8th St., Greeley, Colo.; No. 163, John Henry Wright, 122 E. 42nd St., N. Y. C.; No. 164, W. J. McNamara, 501 Madison St., Maywood, Ill.; No. 165, Horace Mitchell Carter, 115 W. 68th St., N. Y. C.; No. 166, William J. Ohland, 578 No. Maple Ave., East Orange, N. J.; No. 167, Raymond L. McCabe, 8700 Grand River, Detroit, Mich.; No. 168, George Lee, 1310 Matlock Ave., Honolulu, T. H.; No. 169, Samuel P. Slatkoff, 175 Hall Ave., Perth Amboy, N. J.; No. 170, Elder H. Stein, 408 E. 6th Ave., Tarentum, Pa.; No. 171, George F. Young, 3305 Fifth Ave., McKeesport, Pa.; No. 172, James H. Panton, 53 Fruit St., Worcester, Mass.; No. 173, Andrew Boice Anderson, 25 S. 3rd St., Colwyn, Pa.; No. 174, Harold Williamson, Battle Creek Sanitarium, Battle Creek, Mich.; No. 175, J. B. Whitney, Jr., 3216 Gillham Pl., Kansas City, Mo.; No. 176, Abraham T. Schwartz, Naval Hospital, Washington, D. C.; No. 177, Harry G. Danilson, U. S. Naval Medical School, Washington, D. C.; No. 178, Joseph H. Bell, 3011 Seventh St., So., Arlington, Va.; No. 179, George Adam Fox, 2124 Eye St., Washington, D. C.; No. 180, Edwin G. Swann, U. S. Naval Medical School, Washington, D. C.; No. 181, Walter W. McKee, Naval Hospital, Washington, D. C.; No. 182, Frank Robert Bork, U. S. Naval Hospital, Washington, D. C.; No. 183, Leonard Rapoport, 3401 Keswick Rd., Baltimore, Md.; No. 184, Benjamin Frank Allen, 632 W. Lombard St., Baltimore, Md.; No. 185, Paul Taylor Rees, U. S. Naval Medical School, Washington, D. C.; No. 186, Thaddeus V. Niemiec, 1810 W. Chicago Ave., Chicago, Ill.; No. 187, Emma N. Belbot, 1138 Salisbury Drive, Cincinnati, Ohio; No. 188, H. M. Cohen, 3000 Conn. Ave., Washington, D. C.; No. 189, Samuel Ushkow, 210 Throop Ave., Brooklyn, N. Y.; No. 190, William L. Kirschner, 300 West End Ave., N. Y. C.; No. 191, Miguel A. Santos Buch, San Lazaro 299 A, Havana, Cuba; No. 192, Walter M. Kerner, 504 Court St., Elizabeth, N. J.; No. 193, George E. Bolles, 242 Main St., Danbury, Conn.; No. 194, Sister M. Leocadia, St. Elizabeths Hospital, Brighton, Mass.; No. 195, Michael H. Taras, 155 E. Ohio, Chicago, Ill.; No. 196, Nicholas J. Edge, 5401 Chester Ave., Philadelphia, Pa.; No. 197, Marie Rogers, 62 Harrison St., East Orange, N. J.; No. 198, Paul C. Janke, 1658 W. Hopkins St., Milwaukee, Wis.; No. 199, James F. Rieves, University, Miss.; No. 200, Elizabeth D. Dobbs, University, Miss.; No. 201, Jug. John Rosicky, 955/6 Juterpharma, Prag-Modrany, Czechoslovakia; No. 202, Esteban N. Melendez, University of P. R., Rio Piedras, P. R.; No. 203, David Davidson, 2326 So. 12th St., Philadelphia, Pa.;

No. 204, Arthur A. Harwood, 813 E. Jefferson St., Valparaiso, Ind.; No. 205, Oscar Philip Kimmel, 262 St. Nicholas Ave., Brooklyn, N. Y.; No. 206, Teodoro Moscoso, Jr., Plaza Degetau, Ponce, P. R.; No. 207, Shelley Roaten, Jr., 2506 Speedway, Austin, Texas; No. 208, Sister Mary Cecilia Schmefer, 1325 S. Grand Ave., St. Louis, Mo.; No. 209, Ralph R. Kreuer, 1326 Arkansas Ave., Dormont, Pa.

(*Motion No. 36*) Vote on applications for membership in the AMERICAN PHARMACEUTICAL ASSOCIATION.

76. Use of Text of the N. F. VI. The following communication has been received from Chairman DuMez of the Committee on Publications:

> "I recommend that the request of Dr. Robert A. Hatcher of the Department of Pharmacology of Cornell University Medical College be granted, namely, that permission be given the Formulary Committee of the New York Hospital to use portions of the text of the National Formulary VI for comment in a new edition of the New York Hospital Formulary. Since this formulary is intended for the use of the staff and interns of the hospital, I also recommend that no charge be made for this grant."

(*Motion No. 37*) It is moved by DuMez that Dr. Robert H. Hatcher be granted permission to use portions of the text of the N. F. VI in a new edition of the New York Hospital Formulary, with the customary acknowledgment and for value received.

77. Committee on Endowment. President Beal has appointed Dr. Charles E. Vanderkleed as a member of this Committee, to succeed Dr. T. J. Bradley.

78. Committee on Recipe Book. (Council Letter No. 6, page 86, motion No. 19.) Chairman Lascoff recommends that George A. Moulton, Peterboro, N. H., Charles E. McCormick, Baltimore, Md., and M. G. de Navarre, Detroit, Mich., be elected members of this Committee.

It will be recalled that at the recent meeting of the Council, Chairman Lascoff requested the privilege of later recommending several members of the Committee in addition to those elected at that time.

(*Motion No. 38*) It is moved by Lascoff that George A. Moulton, Charles E. McCormick and M. G. de Navarre be elected members of the Committee on Recipe Book for 1936–1937.

E. F. KELLY, *Secretary.*

THE PASSING OF WILLIS G. GREGORY.

HONORARY PRESIDENT OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

Willis G. Gregory, Professor of Pharmacy at the University of Buffalo, School of Pharmacy since 1886, and Dean of the School from 1890 to 1936, died of cerebral hemorrhage at his home in Buffalo, March 20th.

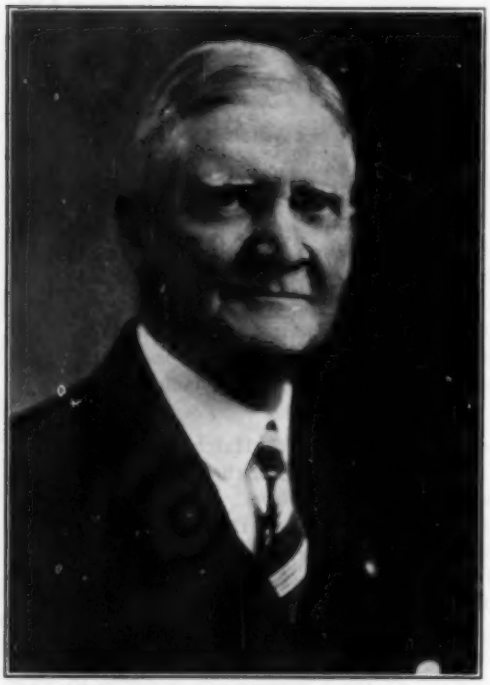
Dr. Gregory was the oldest dean in the profession and widely known for his many contributions to the advancement of pharmacy. During his long career, he held many important local and national positions, such as: Membership on New York State Board of Pharmacy, the United States Pharmacopœia Revision Committee, the National Pharmacy Syllabus Committee and president of the New York State Pharmaceutical Association (of which he was a life member). He held the record of having been a delegate to the U. S. Pharmacopœial Convention for five consecutive terms comprising a period of over forty years, and of having served for thirty-three years as a member of New York State Board of Pharmacy.

He was Chairman of the first edition of the National Pharmaceutical Syllabus Committee.

He was born April 19, 1857, in Theresa, N. Y. The family moved to Amsterdam in 1860 and to Buffalo in 1863.

References to him appear in the April JOURNAL A. PH. A., for 1935, page 259; Volume 1936, pages 374, 476, 840, and elsewhere.

Dean Gregory retired from active deanship of the School of Pharmacy last April, when the faculty and students of the School and the Alumni celebrated their fiftieth anniversary of the founding of the school. At the banquet during the anniversary celebration, his portrait, done in oil, was presented to the School. After his retirement, Dr. A. B. Lemon was appointed to the deanship of the School—see May 1936, page 478. Chancellor Samuel P.



WILLIS G. GREGORY.

Capen paid tribute to Dean Gregory with the following words: "The School of Pharmacy, University of Buffalo, is his creation. His stamp is on it for all time."

In 1885 Dr. Gregory married Gertrude Fargo of Buffalo. He is survived by a daughter, Louise Fargo Gregory of Buffalo, and a son, Francis Fargo Gregory of New York City. Mrs. Gregory died in 1915.

The deceased was a scientist and active in the community and belonged to numerous clubs and professional organizations; among these groups are the Buffalo Torch Club, American Association of University Professors, Metric Association of America, the Mercer Club and the Council of the University of Buffalo; he was member of the AMERICAN PHARMACEUTICAL ASSOCIATION for more than fifty years.

His chief hobby was collecting old mortars and pestles and this valuable collection he gave to the University of Buffalo.

He was *Local Secretary* of the Buffalo meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1924.

CHARLES SONNTAG.

Charles Sonntag, the Spanish War veteran who risked his life in Dr. Walter Reed's famous battle against yellow fever, was honored by the Government January 24th, with a full military burial.

Standing in the falling snow at Arlington National Cemetery, high ranking officers of the Army Medical Corps attended the rites for Sonntag, who died at his Calhoun County, S. C., farm, January 19th, at the age of 64.

Sonntag was the last of the band of men who submitted to the bites of the yellow fever-bearing mosquito in Dr. Reed's experiment to prove the insect carried the disease, Brig. Gen. Jefferson R. Keen, Army Medical Corps, recalled.

"He had the last case of experiment fever at Camp Lezear, Cuba, in 1901," asserted Keen, who was chief Army surgeon in western Cuba at the time.

Dr. Reed's experiment consisted of volunteers submitting themselves to the bite of the mosquito. Those bitten by the mosquito contracted the disease. After he had recovered from the yellow fever contracted from the insects, Sonntag was rewarded with a commemorative medal.

Among the members of the Army Medical Corps who attended were Maj. Gen. C. R. Reynolds, Surgeon General of the Army; Col. James E. Fife, Col. William R. Sheep, Maj. Gen. Merritt Ireland and Col. E. E. Jones.

The widow of the deceased is totally blind.

CLARENCE O. BIGELOW.

Clarence Otis Bigelow, member of AMERICAN PHARMACEUTICAL ASSOCIATION, president and treasurer of C. O. Bigelow, Inc., Apothecaries, New York City, died March 28th.—See February JOURNAL, page 190. Sketch will be published in April JOURNAL.

EDITORIAL NOTES

UNITED STATES CONSTITUTION SESQUICENTENNIAL CELEBRATION.

Organizations have been invited to participate in the sesquicentennial celebration, among them the AMERICAN PHARMACEUTICAL ASSOCIATION. The occasion is to be observed this year.

PHARMACISTS IN THE ARMY.

The committe of the council of the Pharmaceutical Society, Great Britain, reported that they had received a report from Professor Gunn concerning conversations which had suggesting directions in which the War Office might be further approached on this question, and had remitted these proposals to a subcommittee for further consideration. The subcommittee had also been requested to examine the motion proposed by Mr. McNeal—"That a Corps of Pharmacists be established and trained in those duties which they would be called upon to perform in the event of war while serving with His Majesty's Forces."

The term "dispenser" or "dispensing chemist" for certain appointments held by pharmacists is to be substituted by "pharmacist." The secretary was instructed to communicate above information to the British Hospitals' Association in respect of voluntary hospitals, the Ministry of Health and the Wholesale Drug Trade Association.

A communication was read from the *Deutscher Apotheker*-führer relative to the possibility of arrangements being made between England and Germany for interchange of pharmacists, for limited periods, for the purpose of gaining experience. A similar inquiry came privately to the secretary from Switzerland.—The above is abstracted from the "London Letter" to the *Australasian Journal of Pharmacy* for January.

THE STIMULATION OF PLANT GROWTH.

The modern discovery that drugs can be administered as it were through the stem in homeopathic doses is one of considerable interest and importance. This was foreshadowed some twenty-five years ago by the work of H. E. and E. F. Armstrong on the leaves of the cherry laurel and the spotted Aucuba, when they showed that a considerable number of substances were able to enter the leaf and initiate changes which, in brief, may be described as altering the water balance of the cell content and setting enzymic changes in motion, resulting in hydrolysis as was made manifest by the destruction of the glycosides. This work was an extension of the earlier and now classic experiments of Adrian Brown on the penetration of the semi-permeable membrane of the barley seed. The more recent observations made in connection with the ripening of fruits has shown that a vapor, proved to be ethylene, produced during ripening, is able to penetrate other partly ripe fruits and thereby hasten the process of ripening. A new discovery involves the application of small quantities of the particular chemical mixed with lanolin, which is smeared on the stem. In this way it is able to penetrate through the differential septa, pass into the cells behind, and initiate chemical changes. If the stimulus is not too vigorous, the result is accelerated growth and particularly the formation of rootlets at or near the infected part, with the very important practical consequence that the formation of roots by cuttings is much facilitated. A discovery which may be of prime importance to practical horticulture has been made.—From *Chemistry and Industry* (England).

NEW AND NONOFFICIAL REMEDIES.

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.—PAUL NICHOLAS LEECH, *Secretary*.

PROTAMINE ZINC INSULIN.—A preparation of insulin modified by appropriate addition of protamine and a zinc salt. When this modified preparation in its precipitated form is brought into uniform suspension, each cubic centimeter contains 40 units of insulin together with from 0.30 to 0.50 mg. of protamine and from 0.08 to 0.10 mg. of zinc. The preparation contains, in addition, sufficient disodium acid phosphate to maintain its hydrogen-ion concentration at not more than that corresponding to $p_H = 7.1$ and not less than that corresponding to $p_H = 7.4$. This buffering agent, in terms of its anhydrous salt (Na_2HPO_4), represents not less than 0.15 per cent and not more than 0.20 per cent of the final product. The preparation also con-

tains approximately 1.6 per cent of glycerin as an agent for achieving of isotonicity, and 0.20 per cent of cresol or 0.25 per cent of phenol as a preservative.

Actions and Uses.—The effects of protamine zinc insulin are as described under Insulin-N. N. R., except that the blood-sugar-lowering action of unmodified insulin becomes maximal in from two to three hours, whereas the blood-sugar-lowering action of protamine zinc insulin is prolonged and has its greatest effect in about twelve to twenty-four hours after administration.

Protamine zinc insulin may be used in the case of any patient where regulation of diet is incapable of removing the cardinal objective symptoms of diabetes mellitus, and may replace, wholly or partly, the use of unmodified insulin in the treatment of the patient. In some cases the use of unmodified insulin alone is desirable; in others, protamine zinc insulin alone is indicated; while in others, the use of both preparations gives best results.

In view of the prolonged action of protamine zinc insulin, the chief indications for its use are in those cases where unmodified insulin is unable to provide control, without being administered in several doses daily, or is unable to provide adequate control unaccompanied by frequent hypoglycemic reactions, ketosis, or evidence of pronounced fluctuations in blood-sugar levels. The usefulness of protamine zinc insulin in cases of diabetic coma, in diabetes complicated by infection, or in the event of surgical operations has not been definitely established. In such instances, therefore, the use of protamine zinc insulin to supplant the use of unmodified insulin is not recommended.

Dosage.—The general principles underlying the administration of protamine zinc insulin are the same as those governing the administration of unmodified insulin (see Insulin-N. N. R.). (The omitted paragraphs may be found in the complete report of the *Journal A. M. A.*, February 20, 1937, page 640.)

In protamine zinc insulin, the insulin component is derived from batches previously tested and approved in their unmodified form; the protamine component is derived from sperm or mature testes of fish belonging to the family Salmonidæ, genus Oncorhynchus, Salmo or Trutta; and the zinc component is derived from a solution of zinc chloride (0.17 mg. of $ZnCl_2$ provides 0.08 mg. of zinc). Protamines are basic proteins of simple composition. These substances are prepared according to methods described by Kossel. (Kossel, A.: "The Protamines and Histones, in Monographs on Biochemistry," translated by W. U. Thorpe, 1928 ed., pp. 18–19.)

Protamine, Zinc & Iletin (Insulin, Lilly).—A brand of protamine zinc insulin.

Manufactured by Eli Lilly and Company, Indianapolis, under license from the governors of the University of Toronto.

Protamine, Zinc & Iletin (Insulin, Lilly), 10 cc.: Each cubic centimeter contains 40 units of insulin, together with protamine and approximately 0.08 mg. of zinc.

Protamine Zinc Insulin.—Squibb.—A brand of protamine zinc insulin.

Manufactured by E. R. Squibb & Sons, New York, under license from the governors of the University of Toronto.

Protamine Zinc Insulin.—Squibb, 10 cc.: Each cubic centimeter contains 40 units of insulin together with protamine and approximately 0.08 mg. of zinc.

Ichthyol Readmitted to N. N. R.—(See page 641, *Jour. A. M. A.*, February 20, 1937.)

SYNTHETIC MENTHOL.

Hiroshi Honguchi, of the Tokyo Industrial Experimental Laboratory, has produced synthetic menthol.

ACACIPETALIN.

Two scientists, Dr. Claude Rimington and Dr. O. G. Backeberg, of Witwatersrand University, have obtained from acacias of South Africa "acacipetalin," an hydrocyanic acid-containing substance. Cattle have been poisoned by eating parts of the plant.

DRUGGISTS AS INTERNS.

Due to a recent amendment to the New Jersey Pharmacy Practice Act, physicians in that state are to place their prescriptions in more expert hands than heretofore. The new amendment demands that a pharmacy graduate serve a one-year internship before he can qualify as a registered pharmacist. Requirements are as follows: Compounding a minimum of 600 prescriptions under the watchful eye of a licensed druggist; supervised filling of at least sixty orders for poison; visiting three to five physicians to discuss prescription dispensing; studying the manufacture and distribution of drugs. Embryo pharmacists must serve their internship in a so-called training pharmacy designated as such by the State Board of Pharmacy. Records of an applicant's career as an intern, compiled by himself and by his employer, must accompany his petition for a license.—From *Medical Economics*.

HOSPITAL PHARMACISTS.

We quote the following from the "Hospital Number" of the *Journal A. M. A.*, page 1047, March 27th:

"A total of 1419 hospitals reported that they employ 1901 pharmacists. Most, or all, of the states of the Union have laws regulating the practice of pharmacy, the handling of drugs in hospitals, as well as elsewhere, and provisions for registry under the state government.

"The Essentials of a Registered Hospital require that 'the handling of drugs should be adequately supervised and should comply with state laws.'"

INORGANIC INSECTICIDES.

"The possibilities for new insecticides among inorganic materials are not being overlooked. Cryolite—'sodium fluoaluminate' to the chemist—has been shown to give adequate control of the codling moth in the relatively dry Pacific Northwest, although it holds out less promise farther east. Unfortunately, fluorine, a component of cryolite, is poisonous to man as well as to insects and its removal from fruits has thus far proved difficult.

"Recent chemical analyses of a large number of commercial calcium arsenates—widely used insecticides that are less objectionable than lead arsenate from the spray residue standpoint and also less effective against most insect pests—revealed great differences in solubility and other characteristics...."—From a Press Bulletin, U. S. Department of Agriculture.

A JOURNAL AND REPRINT LIBRARY IN MAINE.

A journal and reprint reference library is being established at Lewiston, Maine, in the Central Maine General Hospital. Subscriptions have been made for forty-seven journals, and the library is cataloging and filing about 2000 reprints. This library is being established through a grant of the Bingham Associations. It will serve members of the Maine Medical Association, filling requests for loans of journals and reprints, and thus help the members prepare papers to be read before their various medical meetings. Each member of the Maine Medical Association is also requested to send to this library two copies of reprints of papers which they have published or will publish in the future. Requests for literature should be addressed to the Librarian of the Frederick Henry Gerrish Library, Central Maine General Hospital, Lewiston, Maine.—From American Medical Association Organization Section.

DIAMOND ANNIVERSARY OF SWEDISH PHARMACEUTICAL SOCIETY.

From a December number of *Farm. Revy* we learn that on December 6, 1936, a celebration in honor of the 75th jubilee of the Swedish Pharmaceutical Society (Farmaceutiska föreningen) was held in Stockholm with over 200 members in attendance. Among the guests of honor were: T. Thunberg, K. Ahlsberg, E. Ohlsson and G. Edman, also several representatives from pharmaceutical organizations in Norway, Denmark and Finland. The principal speaker, Apothecary S. Gullstrom, delivered an address on the lives of Priestley and Lavoisier, and at the dinner following, among other speeches, the same speaker discussed Scheele's work and proposed a toast to him.—*Courtesy of C. S. Leonard.*

PERSONAL AND NEWS ITEMS.

PROFESSIONAL SERVICE.

Chairman Anton Hogstad, Jr., of the National Pharmacy Week Committee, who has served as Special Assistant to the President, Merck & Co., Inc., during the past six years, and E. H. Rauth, director of advertising and editor of *Merck Report*, have resigned these positions to engage in the establishment of Anton Hogstad Associates at 136 Liberty St., New York City. The firm will render the professionally minded pharmacists of the United States and Canada a distinctive and exclusive type of professional service relative to the planning, conduct and development of American pharmacies.

The activities of Mr. Hogstad are well and favorably known. He planned the Prescription Shop of Hesselberg Drug Company in St. Louis and at other periods was member of the faculties of several schools of pharmacy and for a time served the Missouri Botanical Garden in important undertakings.

BANQUET AND RECEPTION IN HONOR OF DEAN AND MRS. HOWARD C. NEWTON.

The Alumni Association of the Massachusetts College of Pharmacy honored Dean and Mrs. Howard C. Newton at a banquet and reception in the beautiful George Robert White Hall of the College on March 11, 1937. Over 250 alumni and friends gathered for the occasion; among them were, William H. Glover, president of the Massachusetts College of Pharmacy, Dean Hugh C. Muldoon, former teacher of Chemistry at the College and now Dean of the Duquesne University School of Pharmacy, George A. Moulton, president of the National Association of Boards of Pharmacy, John Walsh, president of the Massachusetts State Board of Pharmacy, William B. Shangraw, president of the Vermont State Board, Henry C. Levick, president of the Boston Association of Retail Druggists, Martin Adamo, president

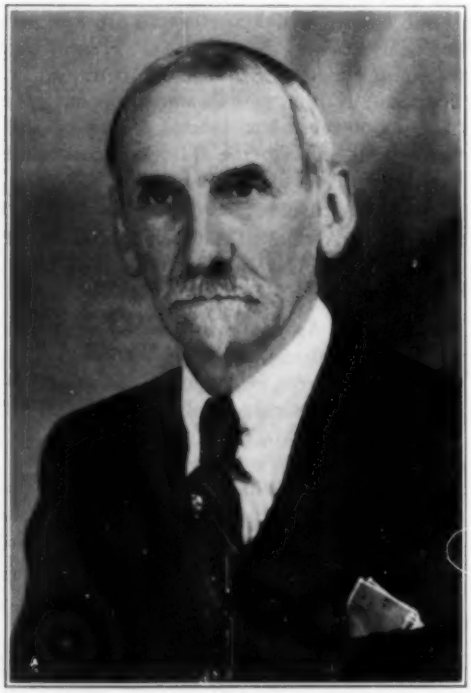
of the New England Drug Council, James L. Case, vice-president of the State Pharmaceutical Association and Doctor G. Edelbert Emard, Governor of the 31st district of Rotary International.

The entertainment included selections by two orchestras, one of which was the 22-piece M. C. P. concert orchestra under the direction of Will T. Bradley, a member of the College faculty. John Camuso of the class of 1925, sang two Italian songs, and Mrs. Ray S. Kelley followed with several numbers.

Secretary Joseph H. Goodness presented the Dean with a beautifully illuminated scroll of welcome which had been signed by over one hundred of the alumni whose names filled all the space available. The Dean, in his address, discussed the future of the College.

Prof. Charles F. Heebner, Dean of the Ontario College of Pharmacy, who has been seriously ill is back at the College.

Professor Franklin T. Green, San Francisco, Calif., will be honor guest at a banquet under the auspices of Pharmacy Chapter of the University of California Alumni Association and the Veteran Druggists' Association of San Francisco at Palace Hotel, May 17, 1937. The General Chairman is Clarmond A. Perry and the General Committee is headed by George H. Frates. Other organizations of pharmacists will participate in the celebration.



FRANKLIN T. GREEN.

Professor Green became a member of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1908. For many years he has been an active association worker; he is Professor Emeritus of the College of Pharmacy, University of California; he has been president of the Veterans' Association for the past ten years. His University connections have been Professor of Analytical and Pharmaceutical Chemistry, Physiological Chemistry in the Medical Department, Chemistry, and Director of the Chemical Laboratories and Dean.

In 1898, he was appointed official chemist, in 1908, toxicologist of the Health Department of San Francisco. He is a former president of California Pharmaceutical Association.

Dr. Lewis R. Thompson, assistant surgeon general, U. S. Public Health Service, has been made director of the National Institute of Health. Dr. Thompson is a graduate of the Louisville Medical College, class of 1905. From 1932 to 1934 he was a scientific director of the International Health Division of the Rockefeller Foundation and is now in charge of the division of scientific research of the public health service. Dr. Walter T. Harrison, senior surgeon in the service, has been placed in charge of the division of biologic control of the institute.

Dr. Daniel J. Posin, instructor in physics in the College of Pharmacy at the University of California, has accepted appointment as professor of physics at the University of Panama. He will sail for Panama in April.

Mrs. Nellie Florence Lee was guest of honor at the annual banquet of the W. O. N. A. R. D., in Philadelphia March 4th. The 80th birthday of the guest of honor was celebrated.

Professor Madame Hideru Suzuki, of the Nippon Women's University, received a degree of the Doctor of Pharmacy, by the unanimous vote of the faculty of the university on November 28th. She is the first woman in Japan who is the holder of the doctoral degree in pharmacy. Dr. Suzuki passed the pharmacist practice examinations in 1918 and later studied in the department of pharmacy of the Imperial University of Tokyo under Professor Heisaburo Kondo. She became a professor at the Nippon Women's University in 1929. Her doctoral thesis covers a study of *Pelilla citriodora* Makino.

OBITUARY.

CARL G. A. HARRING.

Carl G. A. Harring, member of the AMERICAN PHARMACEUTICAL ASSOCIATION and secretary of Pharmaceutical Association Secretaries, died at his home in Newton Center, March 16th.

He was born in Copenhagen and for more than thirty-five years he had been active in American pharmacy. He was a former president of the Massachusetts Pharmaceutical Association and for the last seven years its secretary; a past-president of Boston Association of Retail Druggists and editor of the *Apothecary*. Prior to his retirement, he was for thirty-five years in the drug business in Dorchester.

CARL G. A. HARRING.

He is survived by his widow, Mrs. Mildred E. Harring, president of the Women's Organization of the Boston Association of Retail Druggists, and a son, Dr. Cedric F. Harring.

The deceased devoted his active life to the advancement of pharmacy.

FREDERICK ROHNERT.

Frederick Rohnert, Detroit, Mich., member of the AMERICAN PHARMACEUTICAL ASSOCIATION since 1915, died October 26, 1936, aged 75 years.

In 1882, he opened a pharmacy on Jefferson Avenue, Detroit, which he continued until the time of his death. He was a pioneer pharmacist and took an active part for many years in organization work. He was unmarried.—HENRY R. CARSTENS, M.D.

Emil G. Stucky, 80-year old retired pharmacist, over whose Pittsburgh apothecary shop the one-time destitute O. Henry[1] roomed for a time, died February 25th in Chevy Chase, Md., at the home of his daughter.

Starting at the age of 12, Mr. Stucky became known at 78 as the dean of Pennsylvania pharmacists.

He came to Pittsburgh in 1868. Leaving an apprenticeship at a store in old Alleghany City when he was 21, Mr. Stucky soon opened a chain of business establishments for himself.

He was born in Switzerland in 1856, and the family emigrated to the United States in 1863; and as a youth he entered the drug business. Since his retirement, he lived in Washington.

Funeral services were held in Pittsburgh.

NEW YORK PHARMACEUTICAL ASSOCIATION.

The New York Pharmaceutical Association's U. S. P. and N. F. booklet has been sent to all members of the Bronx County Medical Society, Marty Sasmor reported to the Bronx County Pharmaceutical Association, New York City, at its recent meeting. He also told of plans for a dental formulary booklet and a similar pamphlet for podiatrists. Reporting as chairman of the Trade Committee, Samuel S. Dworkin made a number of recommendations to be acted upon by the association. He has been named chairman of the publication committee. Others to serve with him are Sidney Schumann and Marty Sasmor.

PHARMACY EXTENSION DEPARTMENT, PURDUE UNIVERSITY.

Purdue University, Pharmacy Extension Department, held its 7th annual Druggists Business Conference, March 23rd and 24th.

Plans for the program provided for a number of prominent speakers, among them President George D. Beal of the AMERICAN PHARMACEUTICAL ASSOCIATION.

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[1] A druggist in his earlier years.

SOCIETIES AND COLLEGES.

CANADIAN ASSOCIATION MEETS IN KINGSTON.

The Canadian Pharmaceutical Association and Ontario Retail Druggists' Association will hold their convention at Kingston, Ontario, June 21–24, 1937.

JAPANESE PHARMACY.

A department of pharmacy will be opened April 1st as part of Manchuria Medical College.

The 6th edition of the Japanese Pharmacopœia is to be issued. This is the 50th anniversary.

A committee composed of professors of medicine and pharmacy are making plans for a museum. It will be open to the general public and foreign research workers.

ALLIED PROFESSIONS MEET IN MINNESOTA.

Pharmacists will join with physicians, dentists, nurses and social workers from all over the Northwest for the Congress of Allied Professions which will feature the 84th Annual Meeting of the Minnesota State Medical Association to be held in the St. Paul Auditorium, May 3rd, 4th and 5th.

Leaders in the various professional fields are scheduled to speak before the congress which will open Monday morning, May 3rd, and continue throughout the day with a large public health meeting in the evening as a climax.

Among the distinguished medical men who will address the congress will be: Dr. Maxwell J. Lick, Erie, Pennsylvania, president of the Pennsylvania State Medical Society; Dr. Morris Fishbein, Chicago, editor of the *Journal of the American Medical Association;* and Father M. Schwitalla, St. Louis, president of the Catholic Hospital Association.

Washington representatives of the Social Security Board, the United States Public Health Service, and WPA will also be present to discuss aspects of national welfare activities as they affect the practice of the professions.

RETAIL DRUGGISTS MEET IN AUBURN, ALA.

Vice-President Frank A. Delgado, A. Ph. A., was one of the speakers at the conference of Retail Druggists held at Auburn, Ala. Other speakers of the conference were Dean R. C. Wilson, University of Georgia; L. S. Blake, Auburn Polytechnic Institute, H. S. Noel, Indianapolis; Dean J. W. Scott, School of Science and Literature; A. F. Nickel, Auburn. The meeting was held under sponsorship of Auburn Polytechnic Institute.

AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY.

Professor W. G. Crockett, of the faculty of Medical College of Virginia, former Vice-President of the American Association of Colleges of Pharmacy, succeeds the late Theodore J. Bradley as president of the Association. President Crockett received his early education at Hampden—Sydney College and earned the degree of Doctor of Pharmacy at Columbia University. Before joining the faculty of the Medical College of Virginia he had experience in Industrial Chemistry research and was for a time member of the faculty at Baylor University, Dallas. During the World War he served with the Analytical Research Division, Chemical Warfare Service.

ASSOCIATION MEETINGS.

All officers of Oklahoma Pharmaceutical Association were unanimously reëlected after receiving high acclaim for their accomplishments. The reëlected officers are: Jess W. Stunkle, Enid, *President;* B. M. Jones, Tulsa, *Vice-President*, representing the eastern half of the state; Dave M. McLemore, Britton, *Vice-President*, representing the western portion; Elbert R. Weaver, Stillwater, reëlected *Secretary* for a fifth term, and G. C. Cooper, Edmond, *Treasurer* for a seventh term.

New Hampshire Pharmaceutical Association will hold its annual meeting, September 12th–14th, at the "Balsams," Dixville Notch.

South Carolina Pharmaceutical Association will convene in Charleston, June 8th and 9th, John Frierson, *Chairman* of the Committee on Arrangements.

PHILADELPHIA BRANCH, A. PH. A., ELECTS OFFICERS.

The following officers were elected by Philadelphia Branch, A. Ph. A.: *President*, H. Evert Kendig; *First Vice-President*, S. H. Kerlin; *Second Vice-President*, George E. Byers; *Secretary-Treasurer*, Arthur K. Leberknight; *Delegate to the House of Delegates*, Ambrose Hunsberger.

Dr. A. G. Du Mez was a speaker at the meeting of the American Pharmaceutical Manufacturers' Association in St. Petersburg, Fla. His subject was "Research."

MEETING OF DISTRICT NO. 2, N. A. B. P. AND A. PH. A.

New York Branch of the A. PH. A. was host for District No. 2, N. A. B. P. and A. A. C. P., held at Hotel Pennsylvania, New York City, March 8th–9th. Among many reports and papers were the following:

Adley B. Nichols expressed the opinion that the number of failures before state boards was too high and called for serious study. He did not think that high school graduation was sufficient preparation for the study of pharmacy and suggested that maybe one year in a standard college of liberal arts might be desirable as an essential prerequisite.

Curt P. Wimmer presented an exhaustive review showing a study of the activities of colleges and boards as reflected by resolutions of the past ten years.

Among others, the following presented papers: Wortley F. Rudd, A. G. DuMez, John J. Debus, Frank H. Eby, Charles J. Fuhrmann, H. R. Rudy and Lyman D. Fonda.

J. Leon Lascoff opened the conference with a greeting to the visitors. Chairman Hugo Schaefer had charge of the entertainment program.

MINNESOTA PHARMACEUTICAL ASSOCIATION.

Dean Emeritus Frederick J. Wulling, of the College of Pharmacy of the University of Minnesota, will direct the scientific and practical section at the annual convention of the Minnesota State Pharmaceutical Association to be held here at the Hotel St. Paul on April 5th to 9th. Dr. Bernard Fantus of Chicago will be a guest speaker.

AMERICAN PHAMACEUTICAL MANUFACTURERS ASSOCIATION.

The officers of American Pharmaceutical Manufacturers' Association are: *President*, George R. Flint, Decatur, Ill.; *First Vice-President*, Carroll Dunham Smith, Orange, N. J.; *Second Vice-President*, J. C. Fausnaught, Worcester, Mass.; *Secretary*, C. W. Warner, Newark, N. J.; *Treasurer*, Frank A. Mallett, Des Moines, Iowa. *Members of the Board of Directors:* H. B. Johnson, Pittsburgh, Pa.; E. T. Kirkland, Decatur, Ill.; B. L. Maltbie, Newark, N. J.; Carl N. Angst, Indianapolis, Ind.; Eliot S. Frosst, Montreal, Can.; R. Lincoln McNeil, Philadelphia, Pa.; S. B. Penick, Jr., New York City; R. R. Patch, Boston, Mass.; B. F. Ascher, Kansas City, Mo.

OKLAHOMA PHARMACEUTICAL ASSOCIATION.

Katherine Searle, Red Rock, won the annual Rho Chi junior scholarship award, and Walter P. Scheffe, Enid, was presented the Galen certificate of honor at the annual Oklahoma University Pharmaceutical Association's fourth annual convention.

The Rho Chi award, presented by the campus chapter of the national pharmaceutical society, is given to the junior pharmacy student making the highest grade average during his first two years in the university.

The Galen certificate is given by the leadership society for pharmacy students to the sophomore pharmacist making the highest scholastic average during his freshman year. Scheffe won the award.

Burney Brasel, Drumright, was elected to succeed Bill Cates, Atoka, as president of the association. Val Adams, Oklahoma City, was reëlected honorary president of the group.

Other officers elected were: Raymond Rice, *Vice-President;* Esther Blackmer, *Secretary;* Ray Shaw, *Treasurer;* Burton Hull, *Chairman* of the Program Committee; Ophard Baker, *Chairman* of the Committee on Public Relations; and Jess Tidmore, *Chairman* of the Sports Committee.

Other chairmen elected were: O. Baker and R. Rice, respectively, *Chairman* and *Secretary* of the practical pharmacy section. Andra Kraker and Miss Blackmer were elected to head the section on commercial interests; J. Tidmore and W. Montgomery were named to head the scientific section. Stuart Parrish and Bob Colts were elected *Chairman* and *Secretary* of the section on historical pharmacy.

AMERICAN CHEMICAL SOCIETY.

The ninety-third meeting of the American Chemical Society will open for a four-day session at the University of North Carolina on April 12th. Fifteen divisions of the society will conduct symposia in various fields of research and a group of foreign scientific men will report on their work.

FAIR TRADE LEGISLATION.

Recent gains in Fair Trade legislation include the following states: Idaho, Indiana, Kansas, Montana, New Mexico, South Dakota, Texas and Wyoming. Other states have passed Unfair Practices Acts.

LEGAL AND LEGISLATIVE.

SALVAGE DRUGS.

Joe, an erstwhile wholesaler in salvage drugs, was fined $300.00 in Federal Court (Feb. 28th), the Food and Drug Administration reports. This operator was characterized by Federal agents as one of the most persistent operators in the disreputable drug salvage business. Evidence indicated that the goods were obtained in foreclosure, bankrupt or other "distress" proceedings, and ignoring the prohibition against the interstate shipment of medicines carrying false and fradulent curative claims, sold them to customers outside the state.

The conviction of this operator is another step in the cleanup of resurrected stocks of antiquated medicinals, according to the Administration. Texas, the defendant's home state, has been most active in rounding up these articles. In his annual report issued recently, W. G. Cambell, Chief of the Food and Drug Administration, said, "In Texas, where state officials took the initiative, a rapid and thorough campaign brought the destruction of 28 tons, comprising literally thousands of illegal items. As a result of combined State and Federal activities, two of the largest houses dealing in salvage stocks have discontinued that line, and numerous small operators have turned to fields not within the scope of food and drug legislation."

SOCIAL SECURITY BOARD APPROVES ARKANSAS UNEMPLOYMENT COMPENSATION LAW.

Approval of the new Arkansas unemployment compensation law, signed by the Governor of the State on February 26th, was announced by the Social Security Board. Parts of report follow.

"With Arkansas, 36 States and the District of Columbia are now participating in the cooperative Federal-State system of unemployment compensation set up by the Social Security Act. One more State, Wyoming, recently enacted an unemployment compensation law. All told, approximately 18,086,000 industrial and commercial workers are now protected by their state laws against want during future unemployment.

Of the 11 states which have not yet enacted unemployment compensation law all but two, Florida and Illinois, now have such legislation under consideration in regular sessions of their state legislatures, and in Florida and Illinois the subject is being studied with a view to future action.

Approval of a state unemployment compensation law by the Social Security Board means that employers in the state may deduct from the tax on employers of eight or more, levied by the Social Security Act, up to 90 per cent of it, the amounts which they contribute to the state unemployment compensation system, for employment as defined for the purpose of the Federal tax. It means also that the state may receive Federal grants to cover all proper costs of administering its unemployment compensation law, provided the law is certified as establishing efficient methods of administration designed to give workers their full rights under the law. The Social Security Board has already granted more than $6,170,000.00 to states with approved unemployment compensation laws for administration of their systems.

The new Arkansas law, like the large majority of the other state unemployment compensation laws, sets up a pooled state fund to which all subject employers contribute and from which benefits are paid to all eligible unemployed workers irrespective of their former employers. Employers having one or more persons on their pay rolls for at least one day in any twenty weeks during either 1936 or 1937 will contribute to the state fund at the rate of 1.8 per cent of wages payable during 1937 and 2.7 per cent thereafter. Beginning in 1942 a merit-rating provision goes into effect which enables employers with a small labor turn-over to secure a reduction in their contribution rate.

Employees are not required to pay contributions under the Arkansas law. Approximately 114,000 workers are estimated to be covered by the state system, which will begin paying benefits in January 1939. Eligible workers who lose their jobs will receive compensation amounting to 50 per cent of their full-time weekly wages up to a maximum of $15.00 per week and a minimum of $5.00 or three-fourths of their weekly wages, whichever is less. Benefits may last as long as sixteen weeks in a year, depending on the worker's past earnings.

The Arkansas law will be administered by an unemployment compensation division in the newly established State Department of Labor. This department, created by the legislature at the same time it passed the unemployment compensation law, will be headed by a commissioner of labor, appointed by the Governor

In addition to administration of the unemployment compensation law, the commissioner of labor will also be responsible for administration of the state employment service and for all other state labor laws and regulations."

CALIFORNIA LEGISLATION.[1]

S. 98 proposes to prohibit the planting, cultivating, harvesting and processing of "any flowering tops or leaves of hemp or loco weed (cannabis sativa) or Indian hemp" and to make a violation of the prohibition a felony. S. 118 proposes to prohibit the operation or maintenance of a clinical laboratory except under the immediate supervision and direction of a licensed clinical laboratory technologist or of a person holding a valid and unrevoked physician's and surgeon's certificate. The bill proposes to make it unlawful for any person in a clinical laboratory to make any tests or examinations requiring the application of one or more of the fundamental sciences, such as bacteriology, biochemistry, serology and parasitology, unless he possesses an unrevoked certificate, issued by the state board of health, as a qualified technician in the subject or subjects concerned with the tests or examinations, or possesses an unrevoked certificate as a clinical laboratory technologist, or is the holder of a valid unrevoked physician's and surgeon's certificate. The state board of health is authorized to license as a clinical laboratory technologist (1) any person who for more than five years has been engaged actively in the work and direction of a clinical laboratory and (2) any other person who is found to be properly qualified, by written, oral and practical examination. The board is to be authorized also to license as a clinic or laboratory technician (1) any person who for three years has actively engaged in performing tests in a clinical laboratory and (2) any other person found by it to be properly qualified, by written, oral and practical examinations. S. 121 to supplement the insurance code, proposes to authorize insurance whereby the insurer will provide medical and hospital services, in case of need, to regulate the conditions under which such insurance may be written, and to require the licensing of persons writing such.

CONNECTICUT.

H. 1447 proposes to prohibit the retail sale of barbital or any hypnotic or somnifacient drug except on the written prescription of a licensed physician, dentist or veterinarian. The term "other hypnotic or somnifacient drug" is to include trional, sulfonal, tetronal, paraldehyde, chloral or chloral hydrate and chlorbutanol.

[1] From *Journal A. M. A.*

BOOK NOTICES AND REVIEWS.

Manual of Biological Assaying, By JAMES C. MUNCH, B.S., M.S., Ph.D., Professor of Pharmacology and Bioassays, Temple University School of Pharmacy. Published by J. B. Lippincott, Philadelphia, 1937, 180 pages. Price, $2.00.

Although several books on bioassays have appeared previously, the manual on this subject by Professor Munch is the first of its kind to consider at length the particular causes for success or failure in the biological measurement of drugs according to both official and unofficial methods.

The manual provides for the keeping of data in systematic order through blank or printed forms which are inserted following the description of the method of bioassay.

The final chapter, which considers the evaluation of results by means of mathematics gives a list of important references to bioassay, and adds greatly to the value of the publication.

The book was prepared to meet the needs of the bioassayist, the student and the teacher, and it is predicted that it will fulfil the expectations of the author in this regard.—G. B. R.

Principles of Pharmacy (*Fourth Edition*) By HENRY V. ARNY, Ph.M., Ph.D., Dean and Professor of Chemistry in the College of Pharmacy of Columbia University; sometime Dean and Professor of Pharmacy in the School of Pharmacy of Western Reserve University; Member of the Committee of Revision of the United States Pharmacopœia, Eleventh Revision; Member of the Committee of Revision of the National Formulary, Sixth Edition. With the collaboration of Robert P. Fischelis, B.Sc., Ph.M., Phar.D., Secretary and Chief Chemist, Board of Pharmacy, State of New

Jersey; sometime Dean and Professor of Pharmacy, New Jersey College of Pharmacy; Special Lecturer, Philadelphia College of Pharmacy and Science. 1139 pages with 298 illustrations. W. B. Saunders Company, 1937, Philadelphia. Cloth, $8.00 net. Review, later.

Parenteral Therapy. By WALTON FORREST DUTTON. Published by Charles C. Thomas, Springfield, Illinois, Baltimore, Md. Price, $7.50.

Cosmetic Dermatology. By HERMAN GOODMAN, M.D., with a foreword by S. L. MAYHAM, Editor, *The American Perfumer and Essential Oil Review.* 591 pages, 6 x 9. Price, $6.50. This book provides a systematic discussion of the ingredients of cosmetic preparations, giving the cosmetic manufacturer and his staff, dermatologists and others, a wealth of facts and data on the properties, actions, etc., of these ingredients and a sound basis of consideration for their use in preparations intended for the hygienic or remedial treatment of the skin, scalp, hair and nails. Formulas for more than 1200 shelf-tested preparations. McGraw-Hill Book Co., Inc., New York.

A Manual of Pharmacology. Its Application to Therapeutics and Toxicology. By TORALD SOLLMANN, M.D., Fifth Edition, 1190 pages, illustrated. Cloth, $7.50. Published by W. B. Saunders Co., Philadelphia, Pa.

Gould. New, Medical Dictionary. 4th Edition. 273 illustrations. Flexible Fabrikoid, $7.00. With Thumb Index, $7.50. By GEORGE M. GOULD, A.M., M.D., Edited by R. J. E. Scott, M.A., B.C.L., M.D., and C. V. Brownlow. This new edition contains about 174 tables including a new table on prefixes and suffixes; bacteria. Published by P. Blakiston's Son & Co., Inc., Philadelphia, Pa.

Clayton. Theory of Emulsions and Their Technical Treatment. 3rd Edition. 91 illustrations. 458 pp. Washable Cloth, $8.00. By WILLIAM CLAYTON, D.Sc., F.I.C., Chief Chemist and Bacteriologist, Crosse and Blackwell, Ltd. (London). This work has been entirely rewritten and there is a noteworthy increase in the amount of material it contains. P. Blakiston's Son & Co., Inc., Philadelphia, Pa.

American Red Cross First Aid Text-Book. 110 illustrations. 237 pp. Paper Covers, $0.60, Cloth, $1.00. Prepared by the First Aid Service of the American Red Cross, for the instruction of First Aid Classes. P. Blakiston's Son & Co., Philadelphia, Pa.

Hackh. Chemical Dictionary. 232 illustrations. Over 100 tables. 8 vo.; 790 pp. Fabrikoid, $10.00. Pronunciation and encyclopedic definitions of chemistry terms and pertinent branches of science. By INGO W. D. HACKH, Ph.C., A.M., F.A.I.C., Professor of Chemistry, College of Physicians and Surgeons (School of Dentistry), San Francisco.

Chemical Plant Physiology. 46 illustrations. 497 pp. Cloth, $6.00. Authorized Edition in English. With Editorial Notes, translated and edited by CHARLES J. LYON, Ph.D.

The Chemistry of the Hormones. By BENJAMIN HARROW, Ph.D., Professor of Chemistry, The College of the City of New York and CARL P. SHERWIN, D.Sc., M.D., Dr. P.H., on the staff of St. Vincent's Hospital and French Hospital, New York City. Cloth: 6 x 9. v + 222 pages. Bibliography. Index. Price, $2.50. The Williams & Wilkins Co., Baltimore, Md.

Pharmaceutical Dispensing. By WM. J. HUSA, Professor and Head of the Department of Pharmacy, University of Florida. New Prescriptions, Modern Illustrations, written in a clear, lucid style; incompatibilities scientifically arranged; treats dispensing from a modern scientific and professional standpoint; chapters on professional pharmacy, dental pharmacy, hospital pharmacy, detailing the doctor; thirty-five chapters. Price, $4.00. Husa Brothers, Iowa City, Iowa.

Review of Pharmacy. Fourth Edition. By GEORGE W. FIERO, Assistant Professor of Materia Medica at the University of Buffalo. Price, $2.00. The book is based upon the eleventh revision of the U. S. Pharmacopœia and the sixth edition of the National Formulary. John Wiley & Sons, New York City.

(To be continued.)

THE PLANT SCIENCE SEMINAR.

The Plant Science Seminar held its annual meeting from August 17 to 21 (1936) at a camp in the San Bois mountains, nine miles north of Wilburton, Oklahoma. (See program in June JOURNAL (1936), pages 567–568.) The next seminar will be held in the East, probably on the Jersey coast. Officers elected for 1937 are: *President,* L. K. Darbaker, University of Pittsburgh; *Vice-President,* Elmer H. Wirth, University of Illinois; and *Secretary-Treasurer,* Loyd E. Harris, University of Oklahoma.

"FIRST AID WEEK."

PREPARE for "First Aid Week," May 16th to 22nd. Use the occasion as a means of service and for advancing professional pharmacy.—See page 285.

1937 CENSUS OF PHARMACEUTICAL RESEARCH.

BLANKS HAVE been mailed to pharmaceutical research workers in connection with the 1937 Census Report. Those engaged in pharmaceutical research who have not received such blanks are requested to write for them directly to the Chairman, 40 N. Maple Ave., Lansdowne, Pa., stating the laboratory in which they are working and the nature of research under way. This information is requested in order to prepare a complete report.—JAMES C. MUNCH, *Chairman*.

FIRST U. S. P. SUPPLEMENT DELAYED.

THERE HAS been a slight delay in the issuance of the U. S. P. Supplement, due to changes in plans for the binding. It was originally proposed that the "First Supplement" would be issued with a stout paper cover and that this would be enclosed in a strong spring-back binder capable of also holding such future Supplements as would be issued.

Now, however, to make the "Supplement" less costly it has been decided to offer it without the spring binder, although the binder will still be available for those who desire it. The purpose of the spring binder has been to keep all "Supplements" together and in such form that they may stand on the shelf by the original Pharmacopœia, or be serviceable in the laboratory. With this change in plans the individual Supplement will be bound in a more substantial, but flexible, cover. The proper development of this feature has taken a longer time than was expected.

The Supplement soon to be issued will be known as the "First Supplement to the Pharmacopœia of the United States, Eleventh Decennial Revision." It may not be necessary to issue Supplements annually but these will be published whenever the number of new interim revision changes justify their publication. The delay in the release of the "First Supplement" will no doubt necessitate an advance in the date when the new standards are to become official.

Orders for the "First U. S. P. XI Supplement" should be sent to The Mack Printing Company, Easton, Pa., or to any of the regular distributing agencies for the Pharmacopœia. The price will be $1.00.

W. G. CROCKETT.